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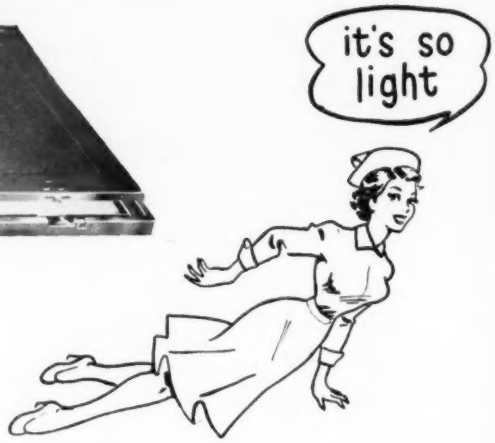

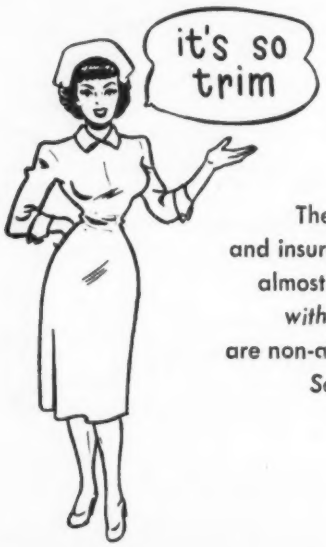

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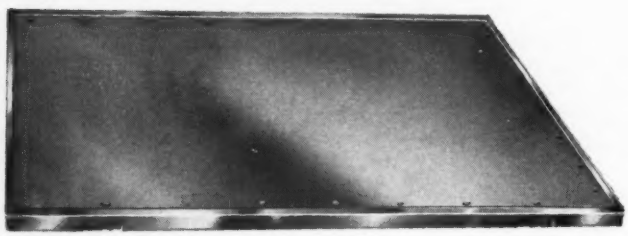

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THE AMERICAN JOURNAL OF ROENTGENOLOGY
RADIUM THERAPY AND NUCLEAR MEDICINE

VOL. 72 SEPTEMBER, 1954 NO. 3

ROENTGEN STUDIES OF THE EFFECTS ON THE SMALL INTESTINE FROM EMOTIONAL DISTURBANCES*

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BECAUSE of tradition, trends in training, and the nature of the roentgen method, diagnostic roentgenologists basically are organologists and give consideration to variation in physiology secondary attention. Fundamentally, this approach is probably correct as our greatest contribution to medicine is to seek out, localize and interpret disease processes as manifested by altered morphology. However, to fully recognize and evaluate organic changes, knowledge of the physiology of the organs examined is essential. Such knowledge of altered physiology alone makes possible early recognition of intrabronchial, nonopaque foreign bodies or small bronchial tumors by the obstructive emphysema found in expiration as there is no structural change otherwise demonstrated. Visualization of the gallbladder and the renal tract are based on the physiology of excretion and concentration of various opaque contrast materials. Certainly it is understood that the radiologist could contribute little information about an organic cardiac lesion if he did not evaluate the physiological mechanics of cardiac chamber pressures in his consideration and interpretation of the morphological changes.

In roentgen examination of the gastrointestinal tract, altered physiological activity largely causes difficulty to the radiologist in search of ulcers, cancers, polyps, inflammatory, and other organic lesions of the intestine by obscuring the structure. The delayed gastric emptying, the pylorospasm and antral spasm, with or without an associated organic lesion in the stomach, must be correctly interpreted. The marked spastic contraction of the colon during a barium enema examination, the presence of marked secretions of mucus on the colonic wall are hazards which make recognition of small tumors of the colon more difficult. Sharply defined, localized and fixed areas of spasm in the colon seen at

* From the Department of Radiology of the University of Minnesota and the Mt. Sinai Hospital, Minneapolis, Minnesota. Presented at the Fifty-fourth Annual Meeting, American Roentgen Ray Society, Cincinnati, Ohio, Sept. 29-Oct. 2, 1953.

times in multiple examinations have been called the filling defects of tumors, and I, among others, to my chagrin, have snapped at that artificial bait. The aforementioned are just a few examples of the great number of physiological variations which are encountered by the radiologist and must be evaluated to avoid errors of false positive organic diagnosis or in missing a lesion.

Following the reports by Mackie *et al.*[12,13,14,15] in 1933 and 1935, and by Snell and Camp[19] in 1934 in which these authors observed "functional changes" in the roentgen picture of the small intestinal mucosa in cases of sprue and chronic idiopathic steatorrhea, a considerable volume of literature has developed concerning these variations in the appearance of the small intestine which are primarily *not due to structural changes in the small intestine but to a variation in physiology*. Snell and Camp originally maintained that these roentgen changes of the small intestine were not specific and could be produced by other conditions. Later, these mucosal pattern alterations were also observed in cases of vitamin deficiency and other nutritional disturbances and were therefore inaptly labeled as the "deficiency pattern" of the small intestine.

Golden[7] organized the thinking on these phenomena and classified the conditions under which the altered mucosal pattern was observed. He believes that these mucosal changes are primarily due to edema within the intestinal submucosa and are secondary to deranged function of the autonomic nervous system. He selected the term "disordered motor function" as the best description of this phenomenon. This terminology has been almost universally accepted, although much difference of opinion exists as to the mechanism producing the varied altered mucosal pattern.

The small intestine exhibiting the roentgen change of "disordered motor function" will show either hypomotility or hypermotility, segmentation clumping of the barium, coarse flocculation of the barium, coarsening and widening of the mucosal folds, and variably distended and contracted loops of small intestine. These findings are disseminated.

Classification of the various conditions alleged to produce the "disordered motor function" pattern in the small intestine is given in Table I.

For many years I have been impressed by the frequency which the "disordered motor function" pattern is seen roentgenographically and the marked infrequency in which clinical vitamin deficiency, sprue and the remaining conditions outlined in Table

TABLE I

THE VARIOUS CONDITIONS ALLEGED TO PRODUCE THE "DISORDERED MOTOR FUNCTION" PATTERN IN THE SMALL INTESTINE

I. Disturbances of Nutrition[7,15]
   - A. Pancreatic insufficiency
   - B. Tropical sprue[14]
   - C. Idiopathic steatorrhea[12]
   - D. Celiac disease
   - E. Hypoproteinemia
   - F. Hypopotassemia
   - G. Vitamin deficiency[13]
   - H. Intestinal parasites (hookworm)[11]

II. Secondary to Organic Disease in Intestine or Mesentery[7]
   - A. Chronic peptic ulcer
   - B. Ulcerative colitis, regional enteritis, tuberculous enteritis
   - C. Intra-abdominal abscesses
   - D. Tumors in intestine or mesentery
   - E. Sclerosing mesenteritis and lipodystrophy of mesentery
   - F. Mesenteric adenitis

III. Dysfunction Associated with Generalized Metabolic Disease[16,17]
   - A. Hyperthyroidism
   - B. Lead poisoning
   - C. Porphyria

IV. Dysfunction Associated with Neurologic Disease[9]
   - A. Diabetic neuropathy
   - B. Pernicious anemia
   - C. Tabes dorsalis
   - D. Vagotomy and sympathectomy

V. Administration of Foodstuffs with Barium[5,16,17]
   - A. Fats especially fatty acid
   - B. Hypertonic saline and sodium bicarbonate
   - C. Carbohydrate

VI. Retention of Fluid and Mucus in the Intestine[7]

VII. Autonomic Blocking Drugs[10]

VIII. Allergy[7]

IX. Emotional Disturbances

1 as causative agents are observed. Emotional distress has been suspected of producing this roentgen picture but never adequately proved.[1]

A recent report of Goin[6] deserves review. Goin studied a white Jewish woman, aged fifty-four, who suffered from attacks of vomiting, abdominal pain and diarrhea for a period of twenty-two years. She had undergone fifteen abdominal operations for this condition with no relief of symptoms. A small intestinal examination which was done after the subsidence of one attack showed a normal mucosal pattern. The patient stated to Dr. Goin that she believed her attacks followed the eating of pork. This patient believed herself emancipated from the rigid Hebrew dietary laws, but Goin conceived the idea that the eating of pork may have produced a subconcsious conflict which manifested itself as an emotional storm with the bowel as the target area. To prove this contention he reexamined the patient at a later date and blended fat free, finely minced pork with the barium suspension for ingestion by the unsuspecting patient. She *showed a normal mucosal pattern, and suffered no symptoms.* A third examination was then done with ingestion of plain barium sulfate suspension. Immediately after the barium had been taken she was offered a small slice of roast pork. Within thirty minutes after eating the meat she experienced violent abdominal pain and *a film of the abdomen showed a striking change in the pattern of the small intestine as compared to the other two examinations.* Here, then, was an objective experiment in the attempt to differentiate the effect of suspected allergy from that of emotional distress on the mucosal pattern of the small intestine. It is of interest to note that, in this case, reproduction of the patient's symptoms occurred with the changes in the pattern of the small intestine as well.

As examples of analogous studies on the effects of emotion on the mucosa of the gastrointestinal tract we are all aware of the classic work of Wolf and Wolff in their book *Human Gastric Function.*[20] These investigators directly observed the changes of the gastric mucosa with changes of mood and emotion in their patient with a gastric fistula, a present-day Alexis St. Martin. These authors[8] and their colleagues also studied the effects of emotional distress on the mucosa of patients with fistulas of the colon. In fact, Dennis,[3,4] when at the University of Minnesota, observed reddening of the rectal mucosa with petechial formation and hemorrhage of the mucosa through the proctoscope in a patient in whom emotional disturbance from fear and anxiety was produced during the examination.

There have been few reports of investigative studies of the effects on the small intestine from emotional disturbances in human subjects. Cannon[2] studied changes in motility of the small intestine in animals during emotional stress in 1929. Roth and his co-workers[18] recently studied the motility of the small intestine during emotional reaction in humans as determined by pressure recordings on a balloon introduced into the small intestine through a Miller-Abbott tube. They produced definite change in motility of the small intestine 7 times in 34 observations on 20 patients. No characteristic pattern of response was found. I have reviewed the work of others who observed motility change in the intestine during emotional stress. I could find no reports in which investigative studies of the small intestinal mucosal pattern in humans were accomplished.

In roentgen studies of the small intestine the great number of factors which influence and produce the pattern of "disordered motor function" complicates the study of any single factor involved. The case of Goin's was unduly complicated by the fact that the various examinations which demonstrated no true allergy but changes due to emotional effects were done on different days; secondly, the time interval between the ingestion of the pork to the onset of symptoms and to the demonstration of changes on the films was slightly prolonged; and thirdly, the ingestion of the food with

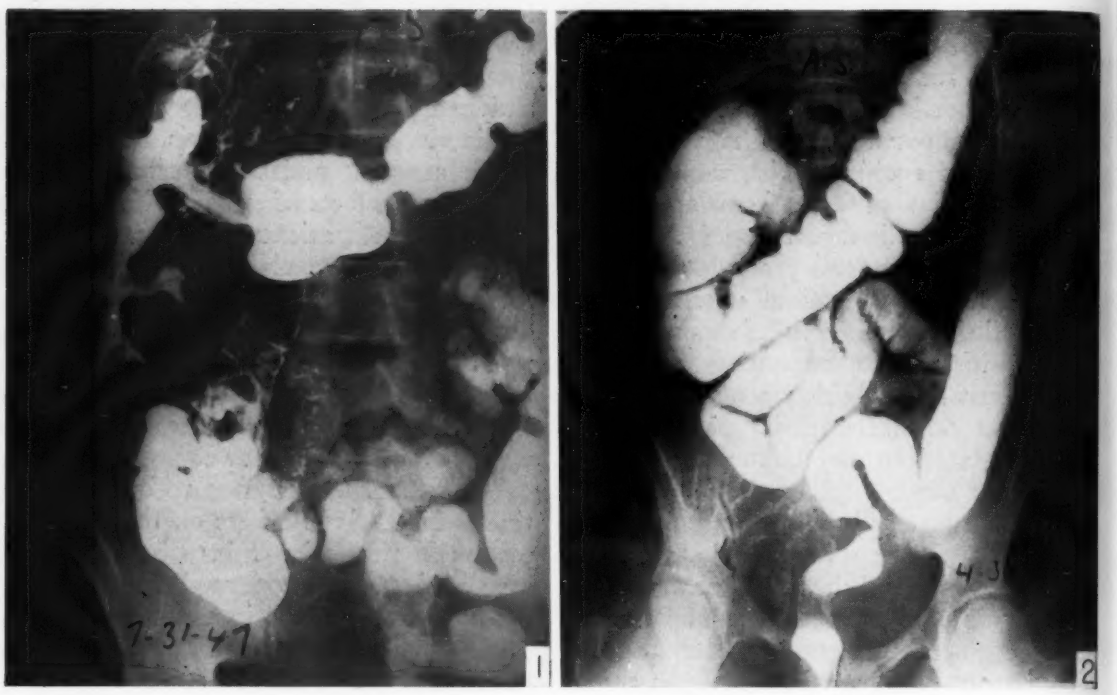

Fig. 1 and 2. Case 1. Fig. 1. Constricting infiltrating inflammatory lesion of the terminal ileum, cecum and ascending colon in 1947 which was later resected. Fig. 2. Rigidity of rectum and rectosigmoid due to ulcerative colitis in 1951.

barium in the stomach could in itself affect the emptying of the stomach and could interfere with the normal small intestinal mucosal pattern.

It was our belief that if we were to attempt to demonstrate the effects only of emotion on the small intestinal mucosal pattern we must adopt a technique similar to any other experiment in which multiple factors affecting similar responses are involved. We must keep all factors constant and vary only the single factor, the effect of which was being investigated. The cause and effect relationship could thus be established.

The plan of the experiment, therefore, was to subject the patient to a small intestinal study with use of plain barium sulfate in water. No additional foodstuffs were to be administered during the procedure. The patient was to remain on the roentgenographic table during the examination. After the recording of a normal mucosal pattern, an attempt was made by interview technique to alter the mood of the patient and to produce an emotional disturbance such as anger, fear, frustration, and self pity. Previous knowledge of the patient's psychiatric background was helpful in producing the desired effect but was not essential. The following four experimental cases studied will be utilized to demonstrate the effects on the small intestine of emotional disturbances.

CASE REPORTS

Case 1. A. S. (No. 4555). This is a white unmarried female, aged thirty-three, with the principal complaint of frequent attacks of diarrhea, abdominal pain and fecal incontinence since 1942. The patient's symptoms started while she was nursing her father following a resection of a carcinoma of the esophagus. At that time her brother also had diarrhea which was diagnosed as ulcerative colitis. The patient's symptoms increased in severity in 1945, and she was treated for ulcerative colitis at the

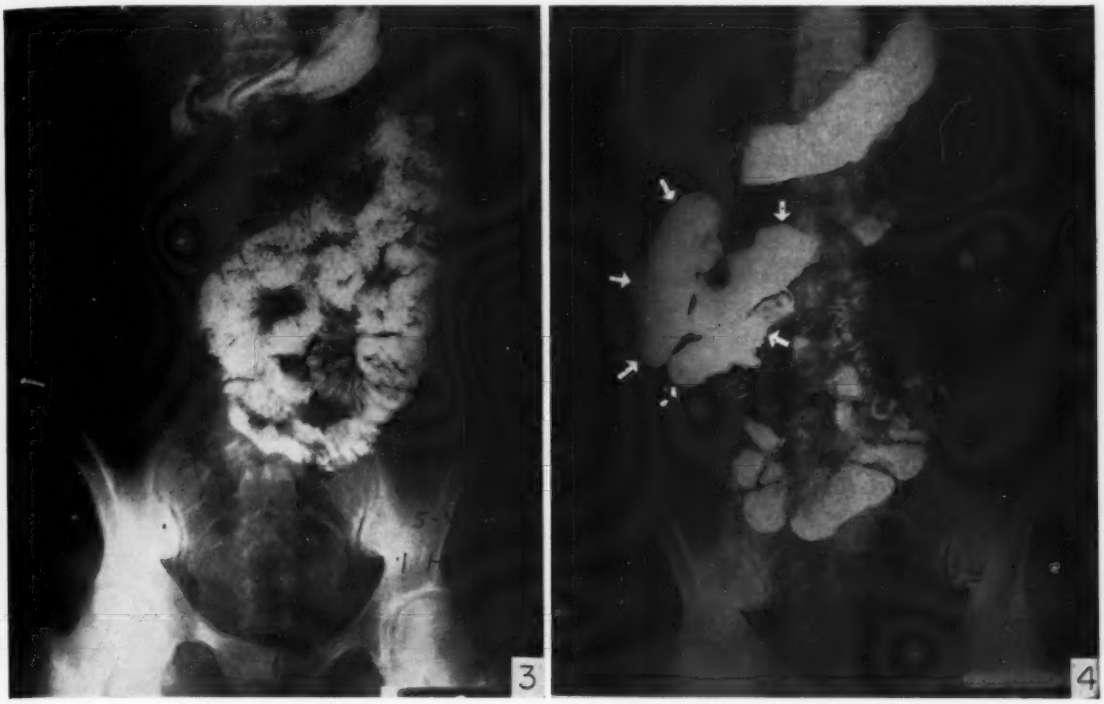

Fig. 3 and 4. Case 1. Fig. 3. One hour film of small intestinal study shows normal mucosal pattern in jejunum. Fig. 4. Film made four hours after original administration of barium sulfate and one hour following second administration of contrast medium. The first ingestion is now clumped in the proximal residual colon (outlined by arrows). The loops of jejunum previously observed to be normal demonstrate disordered motor function on the second administration of barium. The patient was annoyed at the delay in completing the examination.

Mayo Clinic. In 1947, roentgen examination revealed an inflammatory lesion of the terminal ileum, cecum and ascending colon (Fig. 1). A resection of this was done at the Mayo Clinic at that time.

The patient progressed fairly well following this for a number of years, when another episode of diarrhea and severe abdominal pain, bowel incontinence, and bleeding had occurred. She asked to be admitted to the hospital because her symptoms were intolerable and she could not be cared for at home.

The patient was of low intellectual capacity and unattractive physically. During the psychiatric interview she centered mainly about complaints of her diarrhea, the frequency, the quantity, and the quality of her stools. She would describe her stools in much detail and possessed great knowledge concerning what stools should consist of. In fact, she established herself as a connoisseur on stools.

For many years she was hostile to members of her family, mainly to her mother who, she said, was old fashioned and did not understand her. She apparently idolized her father, and upon his death she had an aggravation of her symptoms. She stated that the entire burden of managing the family and providing nursing care for her father rested upon her alone. Her brother neglected his obligations completely. Following her father's death in 1945, her brother managed some real property that was left to her and charged her a management fee which she resented in addition to his other deficiencies. A short time previously she had fallen in love with a newcomer to the community, a displaced person who was the first male to pay her attention. She was happy and free of symptoms during this time until the plans for their marriage. Her fiancé insisted upon a marriage settlement before the ceremony, and on the slow realization she was being married for her small estate rather than her desirability as a wife, her symptoms recurred.

Proctoscopic examination demonstrated atypical areas of redness and ulcerations of the mu-

FIG. 5 and 6. Case 1. Fig. 5. Another small intestinal study demonstrating normal intestinal pattern. Fig. 6. Film made fifteen minutes later, following precipitated emotional disturbance, demonstrates clumping and segmentation of the barium, coarsening of mucosal folds and distention and contraction of loops (disordered motor function pattern).

cosa, and the rectum was long, narrow and not distensible. Roentgen examination of the colon showed a narrowed, constricted and spastic rectum and sigmoid. The haustra of the descending colon were absent (Fig. 2).

On May 4, 1951, a small intestinal examination was done; the patient felt fairly well at that time. The immediate small intestinal films at thirty minutes and at one hour showed normal mucosal pattern and normal distribution of the barium (Fig. 3). An error in management occurred and the patient missed the two-hour follow-up and was brought down for the three-hour film at which the time the major part of the barium was in the colon. An adequate examination of the distal jejunum and ileum was unfortunately not obtained. In an attempt to salvage the examination, another cup of barium suspension was administered. The one-hour film following the second administration of barium showed a difference of mucosal pattern as compared to the one-hour film at the original ingestion of barium (Fig. 4). Certainly, no vitamin deficiency or other lesions had occurred during this short interval. The patient sensed that a mistake had been made and was disturbed by this apparent neglect. It was thought the changes in the mucosal pattern could be due to her annoyance and inconvenience of being without food for an extra length of time.

Another examination was done on May 9 with attempt to see if the changes in the small intestinal mucosa could be produced by the interview technique and better demonstrate the cause and effect relationship of emotional disturbance to the change in mucosal pattern. A record was made of normal mucosal pattern on the one-hour film (Fig. 5). Discussion of the patient's symptoms and psychiatric background was attempted. The patient freely described the resentment she felt toward her mother and brother. Recall of her brother's neglect of responsibility caused her great anger. However, when recall was made to her thwarted love affair, the patient wept. During the course of this conversation, films of the small intestine were exposed at regular intervals. *In fifteen minutes the mucosal pattern of the small intestine was definitely altered from a normal appearance to a characteristic picture of "disordered motor function"* (Fig. 6).

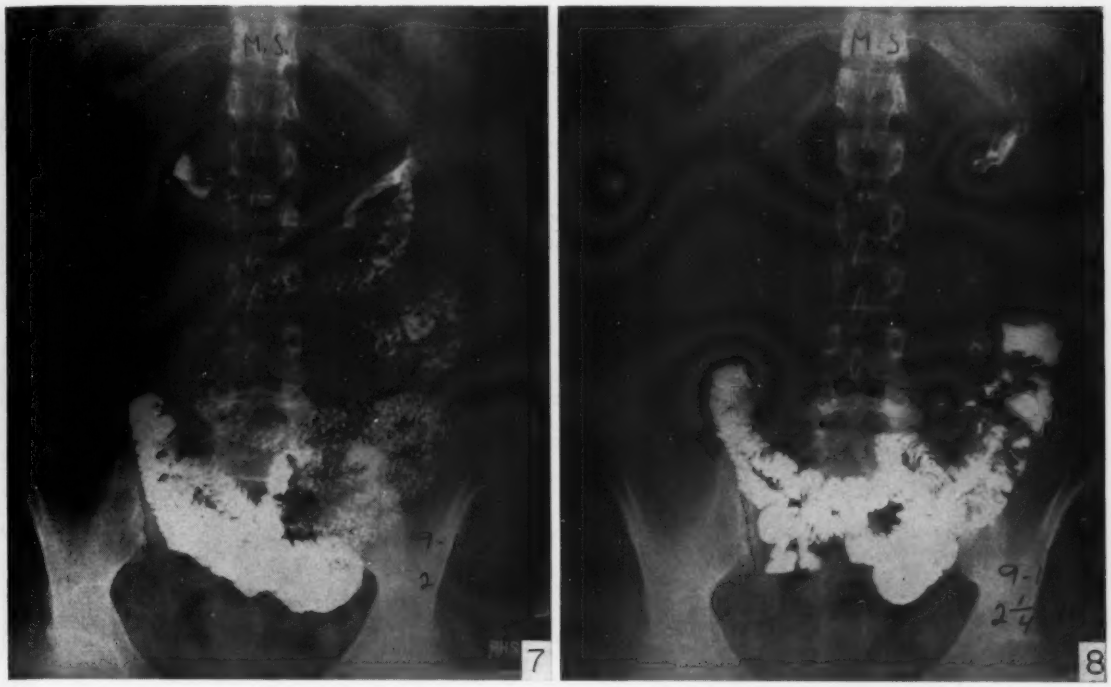

FIG. 7 and 8. Case II. Fig. 7. The two hour film of a small intestinal study shows normal mucosal pattern in jejunum and ileum. Fig. 8. Fifteen minutes later, following precipitated emotional stress, the disturbance of the mucosal pattern is demonstrated.

CASE II. M. S. (No. 5046). This white female, aged thirty-three, presented herself with symptoms of epigastric distress of approximately one year's duration. She stated that she received some relief from pain by the use of milk and food and had periodic freedom from pain for as long as three to four weeks at a time. She had a considerable amount of nocturnal pain, but no melena, nausea or vomiting. In addition, but not concomitantly, she had a one year history of constant right lower quadrant distress with a good deal of rumbling and bloating and feeling of heaviness in her stomach. Physical examination was negative. On August 31, 1951, she was demonstrated to have a duodenal ulcer.

The personality of this individual was known to this examiner inasmuch as she was a secretary in another department of the hospital. She was a voluble, well meaning girl who tried very hard to please, and in doing so inserted herself into everyone's business and vociferously expressed her ideas on any subject at any time whether the listeners were interested or not. Outwardly she did not appear disturbed by the response from many people to these actions, although basically she was a sensitive individual, and it was believed her volubility represented a personality defect for which she was forced to change many jobs and could not keep friends long.

On checkup examination for her duodenal ulcer on January 7, 1953, the small intestinal examination was also accomplished. The one-hour and two hour films demonstrated normal distribution of barium through the jejunum with a normal mucosal pattern (Fig. 7). Interview technique was begun after the two-hour film. It did not take much effort to induce the patient to describe in detail her symptoms. She explained how her illness interfered with her social life and affected her ability to attract a potential candidate for marriage.

In response to questioning of the details of the onset of her illness, she claimed that the abdominal pain came on rather suddenly when she was in New York on vacation the year previously. I asked her what occurred in New York to cause the sudden onset of this pain at that time. The room was darkened for roentgenoscopy and I could not observe the probable blush that occurred on her face, *but within five minutes of intermittent observation roentgeno-*

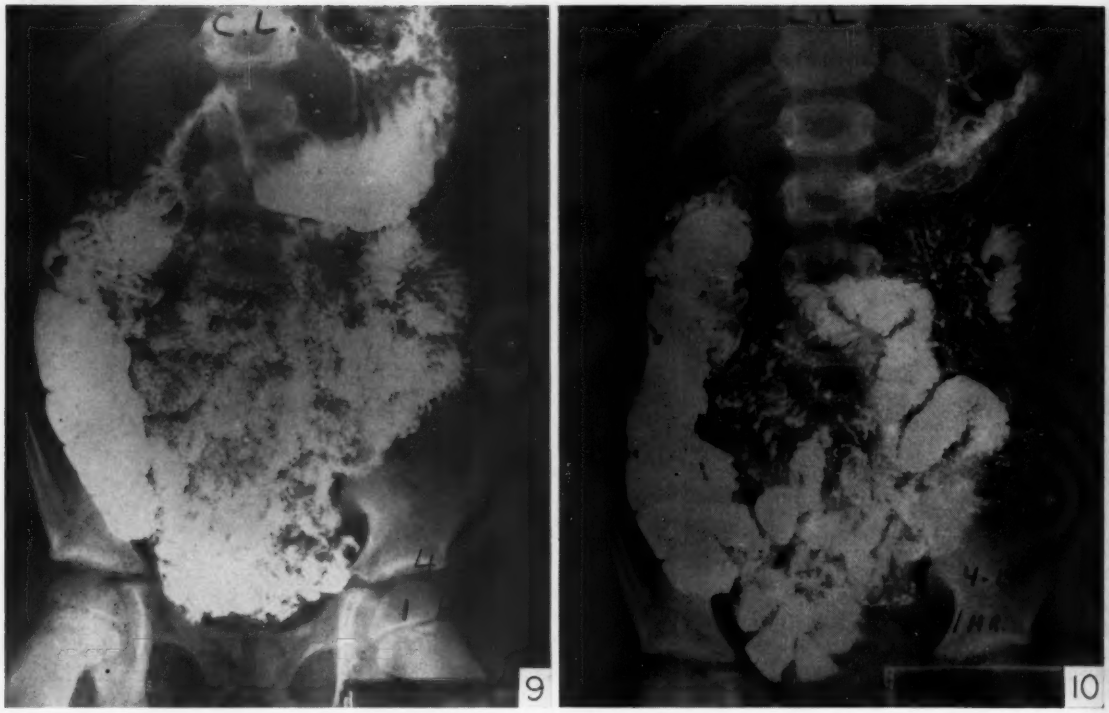

FIG. 9 and 10. Case III. Fig. 9. One hour film of small intestinal study demonstrates fine, lacy appearance of the mucosal pattern of the entire small intestine. Fig. 10. Film exposed twenty minutes later during emotional distress demonstrates the marked change in the appearance of the mucosal pattern.

scopically there was a change in the mucosal pattern of the small intestine recorded on the next film which reached its maximum in about fifteen minutes (Fig. 8). Segmentation, clumping and flocculation of the barium occurred with coarsening of the jejunal mucosal folds. No attempt was made to delve further into the details of the visit to New York.

Case III. C. L. (No. 14950, Mt. Sinai Hospital). This patient is an eight year old white male child who was known to be sickly throughout his life. In past years he had suffered from wheezing on exposure to slight amounts of dust which his mother had called asthma. The child had complained of stomachaches for three years; these vague abdominal pains had no pattern to fit a clinical picture. The pains occurred frequently while at school, necessitating his return home. All these symptoms were due to allergy, according to the mother. Her pediatrician, the referring physician, would not definitely accept this diagnosis, and thought a functional emotional state might be the cause of the distress. The child was allergic on skin testing to house dust and a few uncommon ingestants.

More detailed inquiry into past history revealed that an older sibling of the patient drowned in a creek near the family home when the patient was five months old. Following this the mother adopted an overprotective attitude for the patient to such a degree that she had insisted upon bus service for the patient to school when he was in kindergarten, although other children in the same neighborhood did not receive it. When the school principal became "uncooperative" and refused to extend this privilege, the mother herself brought the child to school every day while the other neighborhood children walked. The child was excused from gymnasium classes and he realized he was different from other boys in his class and could not compete in athletics, as he stated, "I'm not the athletic type." Physical examination was negative. Laboratory examinations were noncontributory. Roentgen examination of the colon on April 1, 1953, was negative.

Examination of the small intestine was undertaken on April 14, 1953. The esophagus, stomach and duodenum appeared normal. There was rapid emptying of the stomach and rapid motility through the small intestine so

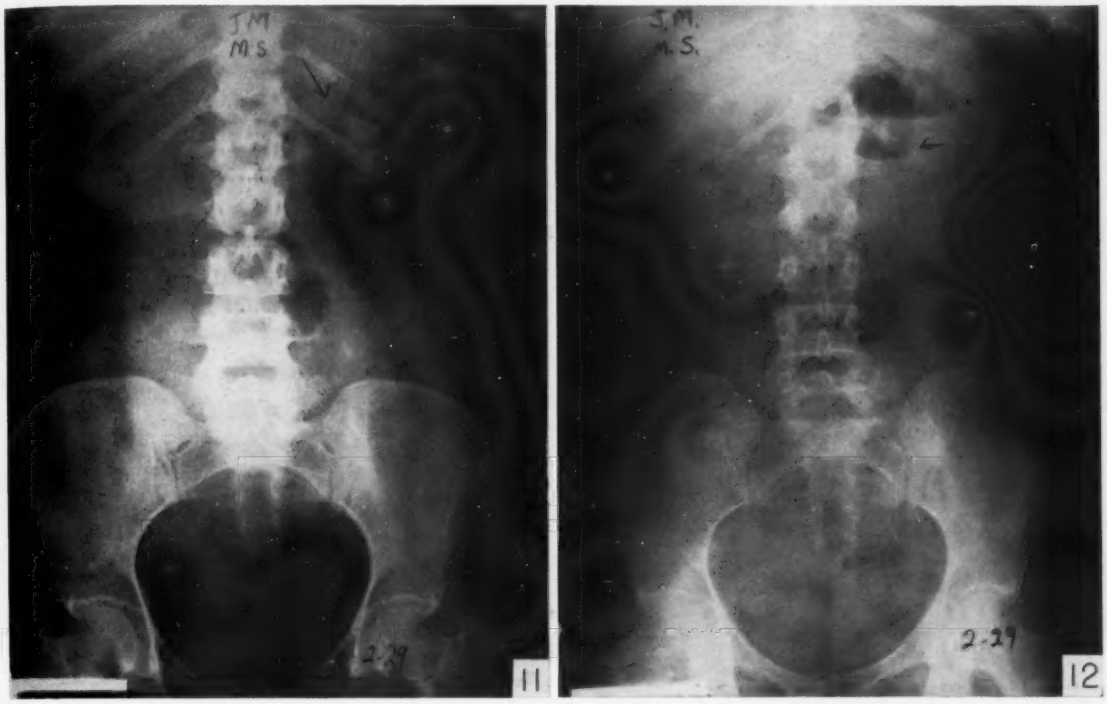

FIG. 11 and 12. Case IV. Supine (Fig. 11) and upright (Fig. 12) films of the abdomen demonstrating absence of gas in the colon, and a hugely dilated fluid and gas containing loop of jejunum in the left upper quadrant with fluid levels suggesting closed loop obstruction of the small intestine.

that in one hour the entire small intestine and the proximal colon were filled. The mucosal pattern of the small intestine was well visualized and uniformly distributed. There was a normal, fine, lacy pattern of the barium and no segmentation was observed (Fig. 9).

Very superficial psychic probing was undertaken by the interview technique while the small intestine was intermittently observed roentgenoscopically. The boy readily revealed that at school he was often beset by a bully who would "make fun of him and push him around." He would make an attempt to defend himself when physically abused, but it apparently was a futile attempt as he stated he always was beaten quickly and forced to run away. The child believed that following some of these fights with the bully he would develop his abdominal pain. Films were exposed ten and twenty minutes following the onset of the interview *and a marked change in the pattern of the small intestine was observed. There was segmentation of the barium, distention of some loops of intestine, contraction of others, widening of the folds, and coarsening of the mucosal pattern* (Fig. 10). *The patient complained of a vague abdominal distress, although he did not actually have pain during the interview and associated with the roentgen findings of "disordered motor function."*

CASE IV. J. M. (No. 7276). This patient is a married white female, aged forty, of Portuguese origin. She was a transient visiting in Minneapolis with the traveling troupe of a Broadway musical production although she herself was not a performer. She was admitted to Mt. Sinai Hospital on February 29, 1952, with a history of severe abdominal pain occurring the day previously which began in the right lower quadrant and later became generalized. The pain was sharp, intermittent, and cramp-like. She had a normal bowel movement the morning before this pain began. The pain persisted through that day and night, and was associated with vomiting and distention. The patient stated that with the cramps she could hear and feel gas in her abdomen. Anorexia was present and she had eaten no food since the onset of the symptoms, and would vomit more than the little liquid she would ingest.

The patient stated that in May of the previous year she had a similar such episode of inter-

Fig. 13, 14, 15 and 16. Case IV. Small intestinal study shows normal mucosal pattern in fifteen minute film (Fig. 13). Film ten minutes later demonstrates change in mucosal appearance and distention of some loops of small intestine previously contracted (Fig. 14). This occurred following precipitated emotional distress. On the two hour film the loops are hugely distended and the mucosal pattern is altered. The patient suffered cramps at this time (Fig. 15). Compare the distended loops of small intestine in the left upper quadrant with those on the original survey film (Fig. 16).

mittent cramps, nausea and vomiting, with increased bowel sounds. Following this earlier attack she was examined at a hospital in Chicago and on roentgen examination of stomach, small intestine and colon, only a diaphragmatic hernia was observed.

On physical examination the abdomen was distended and there was no local tenderness. Borborygmi were heard on auscultation of the abdomen. Laboratory examination was noncontributory.

Roentgen examination on February 29, 1952, demonstrated a few fluid and gas filled loops of small intestine, two of which were remarkably distended. There was only a small amount of gas in the colon. These findings were consistent with a small intestinal obstruction. In view of the large quantity of fluid in these distended and fixed loops of small intestine, the possibility of a strangulating obstruction was entertained (Fig. 11 and 12).

The patient's older daughter, aged twenty-two, who was an understudy to a star performer in this road company, telephoned to discuss the problem. The informant stated that as long as she could recall, when her mother was frustrated or angry, or remarkably disturbed, she would have a similar such episode of vomiting and abdominal pain which would keep her in bed for periods as long as a week. In earlier years she would seldom call a doctor for this complaint, but as she became financially more affluent she could then afford the luxury of medical care during these episodes of abdominal pain.

Her daughter stated that she knew an argument with the patient's most recently acquired husband had occurred the morning of the onset of her present illness. The informant stated, and later this information was confirmed and elicited in more detail from the patient by the surgical resident, that her husband of three months' duration was not well disposed toward her younger children appearing in this musical show, notwithstanding the fact that these children were his means of support. He was jealous of the attention his wife gave her children and he was perturbed because he could not constantly have the privacy he desired. A few days previously he had threatened the patient that he did not like the show, the music, or the cast anyway and was going to return to New York.

The major argument which precipitated her symptoms occurred when she had asked him to take the children for a walk. He violently refused to do this and began to pack his bags vociferously and angrily.

On March 4, after three days of hospital stay, the patient's symptoms had completely disappeared and she was in a good emotional mood. She was brought to the roentgen department and hummed several tunes from the show while waiting. She informed me how much better a singer her daughter was than the star she understudied.

The esophagus, stomach and duodenum appeared normal, and the proximal loop of jejunum filled rapidly and revealed a normal mucosal pattern (Fig. 13), and remained normal until the time the examiner questioned her about the onset of her difficulties. At first she was reluctant to discuss them, and later as a little time passed she described in great detail the argument with her husband and her annoyance at the fact that he would not accept her children, especially when their earnings supported him in a fashion to which he was not accustomed. Within a short time changes in the mucosal pattern became obvious, and in fifteen minutes there definitely was a disturbed mucosal pattern recorded (Fig. 14).

The patient was returned to her room while awaiting later films. Prior to the patient's being brought back for the two hour film, her husband coincidentally cooperated with the experiment when he telephoned her and gave her an ultimatum "to leave the hospital by three o'clock or else." When she returned for the last film she was obviously greatly disturbed, she was crying, complained again of abdominal cramps, borborygmi were heard and the small intestinal mucosal pattern was obviously disordered. There was segmentation of barium in the small intestinal loops with some contracted and some distended loops of intestine (Fig. 15) which compared favorably with the original films of the abdomen made at the onset of her hospital admission (Fig. 16).

We believe we have in this case demonstrated the cause and effect relationship of the emotional disturbance to the distention of the small intestinal loops to the disordered mucosal pattern, and to reproduction of the presenting symptoms of the patient.

DISCUSSION

The significance of the fact that one can produce rapid alteration of the small in-

testinal mucosal pattern under roentgen observation by emotional disturbance requires critical evaluation. Cursory assessment might suggest that herein we have explained the mechanism by which patients so frequently have symptoms without evidence of organic disease in the intestine. Certainly this conclusion is not warranted from the facts that have been presented. Of the 4 cases presented, only in a single case were the symptoms of the patient reproduced in association with the change in the mucosal pattern. In 2 of the 4 cases there was only a vague feeling of abdominal distress associated with the roentgen findings. In other cases examined but not herein reported, no discomfort occurred with minor degrees in alteration of mucosal pattern.

A few supposedly normal individuals with no evidence of intestinal symptoms underwent this examination for evaluation. In one of these, changes of the mucosal pattern were found. However, it is probable that the superficial psychic probing that was done was not sufficient to find an area which actually produced deep emotional disturbance. It must be understood that the psychiatric interview technique was extremely superficial. As it was done by a radiologist and not by a psychiatrist it was felt that meddlesome deep psychic probing by a person unqualified in psychiatry might cause as much harm and damage to the patient as deep probing and cutting by a person unqualified in surgery.

It is believed that these intestinal mucosal changes may conceivably appear in *normal* individuals who are questioned in a way to cause emotional distress such as anger, remorse, fear and frustration and are not necessarily of pathological nature. Certainly, we do not feel that the blush of embarrassment, the increase in blood pressure and pulse rate with fear and anger, and the other normally accepted responses of the body to stress are abnormal findings.

It is conceivable that the described changes in the mocosal pattern of the small intestine could be no more significant than the hyperemia of the blush or the outpouring of tears with emotional disturbances.

Further work is being considered to extend these studies in three directions. First, we plan to evaluate more carefully the subjects psychiatrically so as to probe more deeply and thus create a greater stimulus to the intestine. Secondly, we plan to study the appearance of the intestinal mucosa in patients having enterostomies and correlate the direct appearance of the intestine with the roentgen mucosal pattern. Thirdly, studies will be made to attempt to determine the mechanism by which the altered mucosal pattern occurs.

The results of these studies, therefore, have only demonstrated that emotional distress per se can induce an altered mucosal pattern in the small intestine and that it is not necessary for the patient to be deficient in foodstuffs or chemicals. Nor does the patient necessarily have to be the victim of other diseases; nor do we have to assume that the administration of foods or retention of fluids in the intestine is necessary to produce this pattern. It is probable that emotional disturbances may be the most frequent single etiological factor causing this picture of "disordered motor function" of the small intestine.

SUMMARY AND CONCLUSIONS

1. Roentgen studies have demonstrated that emotional disturbances produced by the interview technique can immediately alter the small intestinal mucosal pattern from a normal mucosal pattern to one of "disordered motor function."

2. Reproduction of the presenting symptoms of the patient was not necessarily always present with the change in the small intestinal mucosal pattern.

3. The altered small intestinal mucosal pattern is not necessarily a pathological entity but may be a functional variation within normal limits.*

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* For discussion see page 408.

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ROENTGEN STUDIES OF THE SMALL INTESTINE IN SPRUE*

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ALTHOUGH the diagnosis of sprue can usually be established by clinical and laboratory methods, the roentgen manifestations in the small intestine in this condition have not been considered sufficiently diagnostic to differentiate from those seen in nutritional deficiency states, allergy, hypoproteinemia, nephrosis, pancreatic steatorrhea and other diseases. Clinical and roentgen observations of a group of patients has led to the concept that there may be a small intestinal pattern characteristic of sprue. The purpose of this report is to analyze the roentgen findings of the small intestine in a group of 40 patients with sprue who have been observed from one to seventeen years: 3 patients were observed for more than fifteen years, 8 for more than five years, 20 for more than three years, and 10 for one year or less. The effect of antianemic and steroid therapy on the roentgen findings of the small intestine will be included, as well as short descriptions of the symptomatology, clinical and laboratory observations.

Plan of Study. Eight patients in this series were studied prior to the administration of any form of therapy. The remainder received some form of therapy before admission to the hospital for study. These patients were observed roentgenologically prior to treatment in the hospital and after treatment which consisted of liver extract, folic acid and vitamin B_{12}. Patients refractory to this form of therapy were given cortisone, ACTH and hydrocortisone (free alcohol).

TECHNIQUE

The small intestine was studied following the administration of a mixture containing 8 ounces of barium by volume to which has been added enough water to make 16 fluid ounces. The first two films were taken at fifteen minute intervals. Further roentgen examination depended on the rate of passage of the barium meal and usually consisted of an examination every thirty to sixty minutes until the barium had left the small intestine. It was occasionally necessary where large segments of small intestine pooled the barium to administer an additional 4 or 6 ounces of the mixture to secure adequate visualization of the small intestine.

Neither saline mixtures nor ice water was administered because these preparations in themselves, in our experience, disturb the small intestinal pattern. Micropulverized barium that we have used has been of no particular advantage: segmentation and secretions did not disappear in patients with sprue following the use of micropulverized barium.[5] Other barium mixtures such as combinations of carboxymethylcellulose with barium also did not affect the small intestinal pattern in sprue. It should be emphasized that every abnormal small intestinal examination should be repeated in order to verify the constancy of the abnormalities.

ROENTGENOLOGIC FINDINGS

Three patients revealed a normal small intestinal pattern. The remainder exhibited in varying degrees the roentgen findings in the small intestine that have been describe by many authors;[11,15,18,22] namely, dilatation, segmentations, thickening of folds, scattering, hypersecretion, fluid levels, moulage sign and motility changes.

Dilatation is one of the most constant roentgen findings in sprue, usually best visualized in the mid- and distal jejunum,

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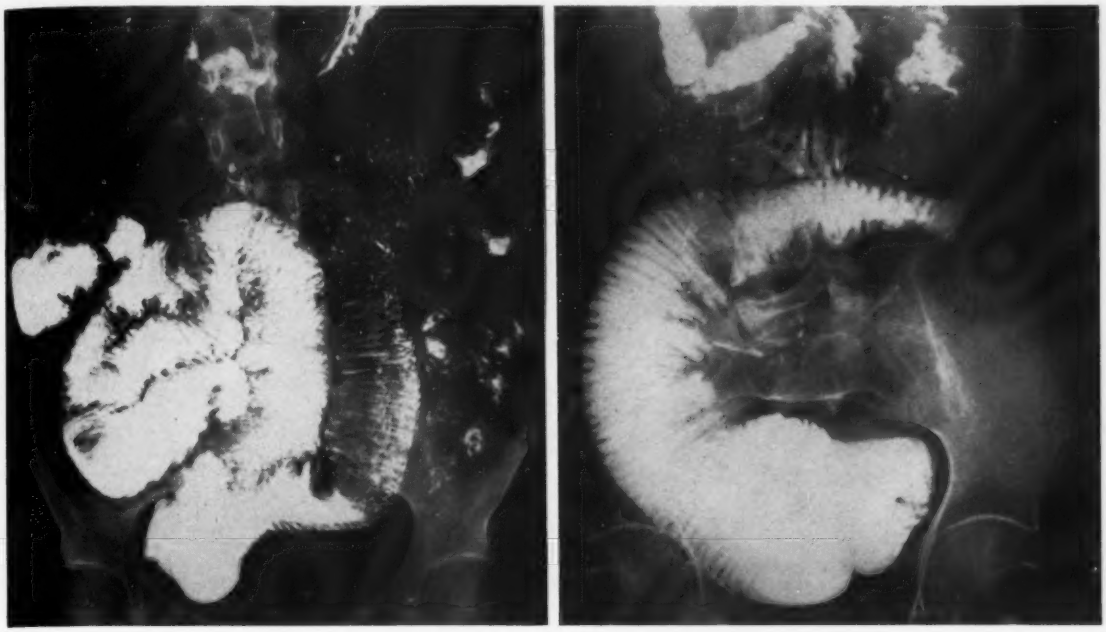

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FIG. 1. (*A*) Moderate dilatation of mid- and distal jejunum, slight delayed segmentation. (*B*) Marked dilatation of the distal jejunum.

though it may be located anywhere in the jejunum or proximal ileum. Dilatation in the distal ileum is not as common as in other portions of the small intestine, Dilatation was found in 33 of 40 cases. The diameter of the normal jejunum has been described as between 2 and 3 cm.[10,15] In this series, 18 cases revealed areas of dilatation that were at least three times the normal; in 14 patients, dilatation was twice the normal, and in 5 patients, the dilatation was mild, approximately one and a half times normal. In general, dilatation appeared to be related to the severity of the disease and was most marked in the more advanced cases (Fig. 1*A* and *B*, 2*A* and *B*). The large intestine may show dilatation (Fig. 3*A*), which can be pronounced and contribute to the development of the volvulus.[14]

The exact cause of the dilatation is unknown. It has been frequently described and the term megajejunum has been given to this finding.[6] The dilatation may be due to several factors, including thinning of the intestinal wall, atonicity, distention with fluid and the mechanical distention of the small intestine, secondary to the large amounts of barium administered. When smaller amounts are used, the dilatation is present, but not as striking. Mechanical dilatation of the normal small intestine has not been observed despite the administration of large quantities of barium.

Electrolyte imbalance, especially potassium deficiency, may also contribute to the marked dilatation of the small and large intestine, seen in severe cases of sprue. Serum potassium values are of no significance as they may indicate normal values, despite a marked potassium depletion. Any patient with prolonged diarrhea, whether due to sprue or other conditions, may develop a potassium deficiency. The administration of potassium to these patients is the only reliable method of determining whether or not potassium is needed. The normal individual would excrete the excess potassium. Dilatation of the small intestine has been produced in animals, following potassium depletion. The exact role of potassium in producing dilatation of the

A *B*

FIG. 2. (*A*) Marked dilatation of mid- and distal jejunum, with thickening of the folds. (*B*) Same patient as Figure 1*B*. Delayed segmentation, increased secretions, huge sausage-like loops, marked fragmentation.

small and large intestine in sprue has not been completely evaluated.[8]

Dilatation of the small intestine is an important feature of the sprue pattern because similar patterns that may be found in association with nutritional deficiencies, nephrosis, hyperthyroidism, pellagra and other disorders are usually not associated with the degree of dilatation seen in the sprue pattern.

Segmentation was seen in 34 patients. It was most pronounced in the ileum and was best seen in the more advanced cases and when associated with hypersecretion. Segmentation may take one of two forms. The first or delayed form presents medium-sized loops of small intestine 4 to 10 cm. in length best visualized in those segments of intestine that are in the process of evacuation or have been most recently evacuated. This was seen on at least one film in each of 26 patients (Fig. 2*B* and 4*B*). These segmented loops also revealed some degree of dilatation (Fig. 2*B*). One patient in whom the disease had been present more than twenty years, the longest duration in this series, demonstrated a barium-filled loop 20 cm. long into which all of the ingested barium had pooled (Fig. 3*B*). The initial dilatation followed by delayed segmentation were two of the most characteristic findings in the sprue pattern.

Four patients presented the second or "early" form of segmentation (Fig. 5*A* and *B*). In these patients segmentation was visualized as soon as the barium filled the small intestine and was seen throughout the entire small intestine. Here, too, the segmented loops are up to 10 cm. in length. This "early" or prompt form of segmentation was in contrast to the "late" or delayed form where segmentation occurs during the process of evacuation as described above. In 2 additional patients a modification of the immediate segmentation was found. These patients presented numerous, small, contracted, barium-filled segments of small intestine 1 to 4 cm. in length, reminiscent of hypertonic, spastic segmentation. This type has been described on occasion in association with allergy, intestinal spasm secondary to hookworm

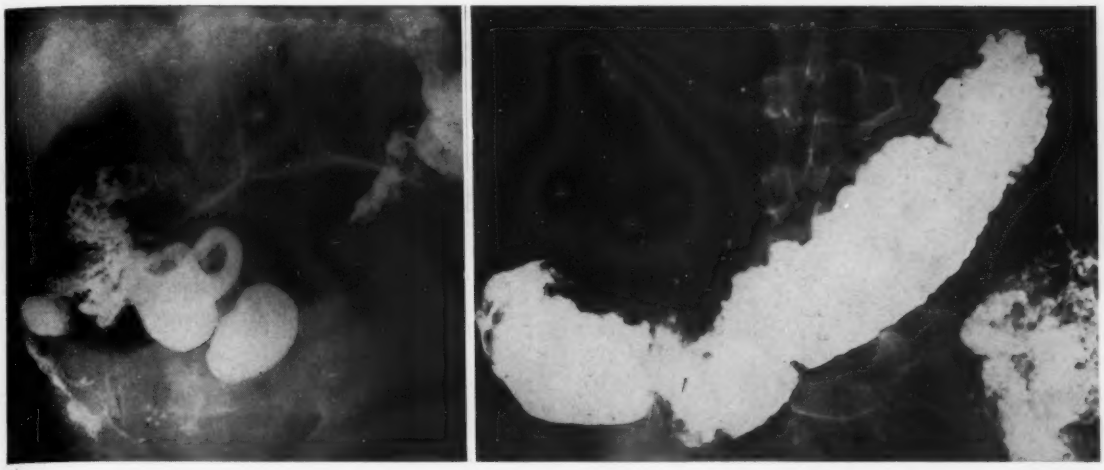

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Fig. 3. (*A*) Marked dilatation of the transverse colon. (*B*) Considerable dilatation of the terminal ileum. Practically all of the barium pooled in this segment of the small intestine, increased secretions.

disease, Henoch's purpura or other related disorders; it has been described also in the lacteal form of Hodgkin's disease. It may be found normally in infants and the aged.

Segmentation is not specific for sprue. It has been noted in lymphosarcoma, Hodgkin's disease, nephrosis, pancreatic steatorrhea, hypoproteinemia, anaphylactoid purpura and in other disorders. It is more than likely that co-existing nutritional deficiencies might have contributed to the development of this pattern in some of these conditions.

Experimentally hypertonic solutions, sodium oleate, and olive oil with free fatty acids were employed successfully to induce segmentation in the small intestine. Isotonic solutions, on the other hand, produced no alteration in the small intestinal pattern.[12,25,29] These induced patterns differ from the sprue pattern because of the absence of significant dilatation in the jejunum and the presence, immediately, of the small, contracted, hypertonic form of segmentation.

The exact etiology of segmentation is unknown. Some authors have attributed the cause to spasm, either neurogenic or muscular.[15,29] Although these factors probably play significant roles, it appears likely that the abnormal quality and quantity of secretions and the presence of excess of fat in the intestine are also important in the production of the segmentation pattern.[12] The cause of the delayed segmentation is difficult to evaluate, but, again, may be due to the inability of the atrophic atonic intestine to properly propel the barium contents in a smooth, normal fashion. Alteration in the parasympathomimetic substances may play an important role.[17] The term flocculation is also used frequently instead of segmentation.

Between the dilated segments of intestine there may be noted irregular, worm-like or string-like strands of barium (Fig. 6*A* and *B*). These collapsed loops of intestine have a peculiar, but fairly characteristic appearance and are usually associated with segmentation. They are inconstant, vary from film to film and appear to be due to a disordered motor phenomenon, related to spasm or incomplete evacuation of a segment of intestine. This abnormal finding was especially noted when numerous films were taken approximately thirty seconds apart.

Hypersecretion. An abnormal amount of secretions in the intestinal tract is a constant phenomenon in most cases showing the sprue pattern (Fig. 2*B*, 3*B*, 5*A* and 6*B*). Gas and fluid levels may be seen oc-

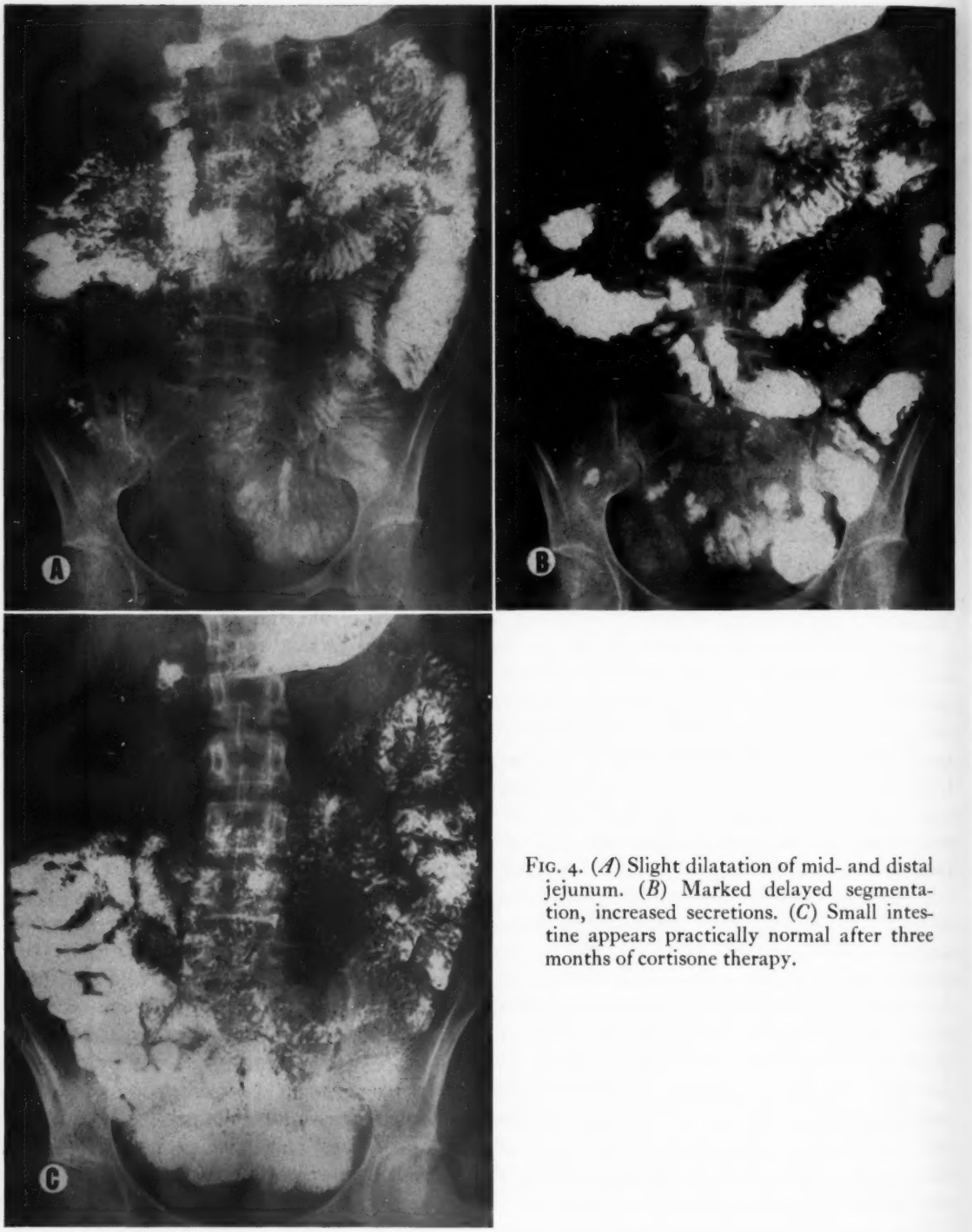

FIG. 4. (*A*) Slight dilatation of mid- and distal jejunum. (*B*) Marked delayed segmentation, increased secretions. (*C*) Small intestine appears practically normal after three months of cortisone therapy.

casionally during the small intestinal study. Hypersecretion varies with the degree of segmentation. The usual homogeneous mixture of barium seen in the normal intestine is absent. Instead, the barium suspension presents a granular quality with areas of coarser flocculation dispersed throughout the barium-filled segment. The flocculation

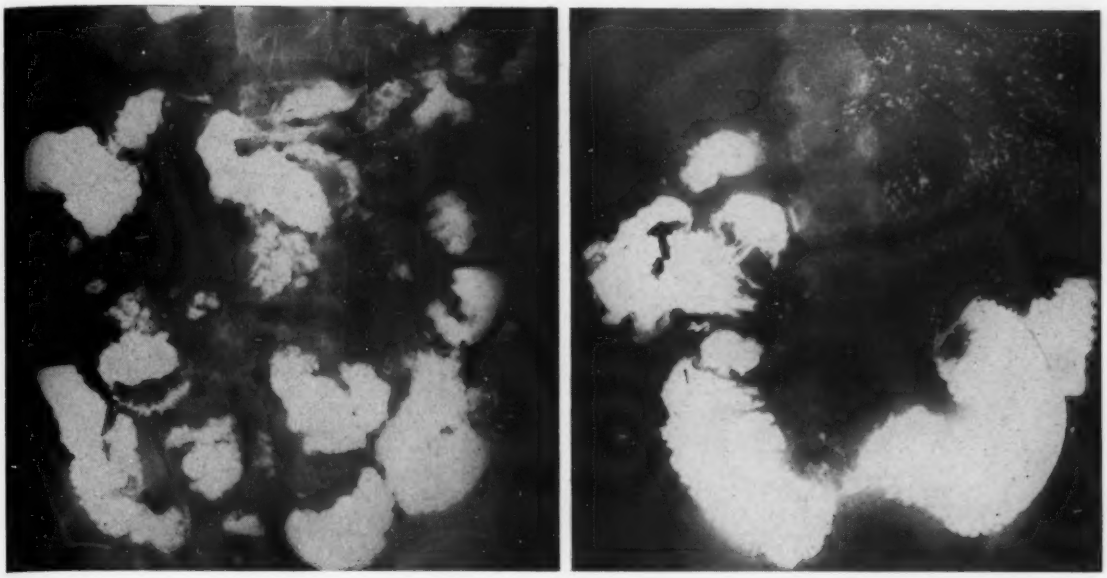

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FIG. 5. (*A*) Early, marked and persistent segmentation, increased secretions, moulage sign. (*B*) Early segmentation, increased secretions, segmentation.

is best visualized on the periphery of the segment. Some observers have produced similar patterns following the admixture of mucus to barium.[5,29] Other authors have emphasized delayed absorption of fluid by the intestine in sprue;[9] this difficulty may be one of the factors responsible for the presence of increased secretions observed in the small intestine following the ingestion of the barium water mixture. It may also be responsible for the immediate dilatation. However, present knowledge of the nature of succus entericus and of its alteration in sprue precludes any adequate explanation of these observations.

Thickening of the folds is best demonstrated in the duodenum and jejunum and is probably a result of many factors, including edema of the mucosa and hypertonicity of the muscularis mucosae. Thickening of the folds was particularly striking in 8 patients, but slight thickening was present in most of the cases (Fig. 4*A*, 6*A* and 7*A*). In 1 patient, the roentgen pattern revealed considerable thickening of the mucosal folds (Fig. 3*A*), yet at autopsy, marked atrophy of the intestinal wall was reported. A case similar to this has been previously reported.[15]

Moulage Sign. The moulage sign was a name originally given to the roentgen appearance of segments of the proximal jejunum in sprue in which the folds appear to be completely effaced. It was described as "resembling a tube into which wax had been poured and allowed to harden."[18] In this series, it was seen in only 6 patients. The moulage sign appears to be related to marked atonicity and atrophy of the intestinal wall and is found in the most advanced cases.

Scattering. As the barium leaves the small intestine a faint irregular stippling of residual barium is occasionally seen along the course of the jejunum. This is a normal finding. However, in the sprue pattern, there was observed a large amorphous mottling 2 to 4 mm. in diameter, resembling snowflakes (Fig. 2*B*). This effect is called scattering and is seen along the course of the jejunum or proximal ileum. This finding was usually associated with pronounced segmentation and an increase in secretions. Two types have been noted which we have termed spotty and linear.

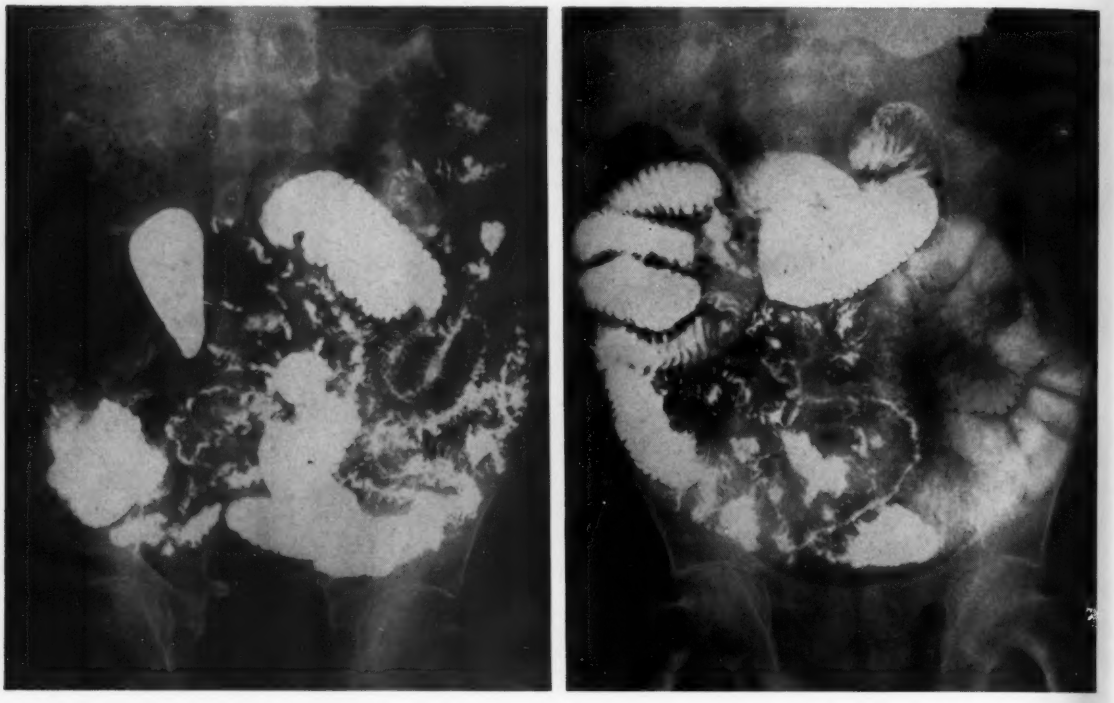

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FIG. 6. (*A*) Delayed segmentation, increased secretions, worm-like collapsed segments of intestine. (*B*) Moderate dilatation, increased secretions, worm-like segments of intestine.

The spotty type resembles snowflakes (Fig. 2*B*, 7*B* and *C*). Linear scattering was the worm-like segment, already described under segmentation (Fig. 6*A* and *B*). In an occasional patient, the scattering was marked, with distortion and thickening of the folds, suggesting considerable irritation (Fig. 7*C*).

Motility. The term "transit time" has been employed to indicate that period required by the barium mixture to reach the cecum following ingestion.[15] In a large series of normals, recently reported, intestinal transit time varied from one to nine hours. The average time in adults between the ages of twenty to twenty-five years was found to be three hours.[21] In 36 patients in this series the transit time was between three and five hours. In 3 patients the barium reached the cecum within one hour; in 1 of these patients the transit time was less than thirty minutes (Fig. 8*A* and *B*).

In 2 other patients the transit time was seven and six hours, respectively. It was interesting to note that in none of these patients was the transit time markedly prolonged. This may be accounted for by the fact, mentioned previously, that the majority of the patients in this series received some form of therapy prior to roentgen examination.

Summarizing the roentgen findings: In 70 per cent of the cases of sprue, the pattern was fairly characteristic, and consisted of immediate dilatation of the jejunum, delayed segmentation in the distal jejunum and ileum, spotty and linear scattering, and increased secretions. In 30 per cent of the cases, one or another roentgen feature described above was unusually prominent, such as segmentation or flocculation, marked thickening of the folds, tremendous dilatation, increased secretions, or unusual hypermotility. In 15 per cent of this latter group, immediate segmentation, which persisted throughout the examination, was the unusual feature. The initial dilatation described above was absent.

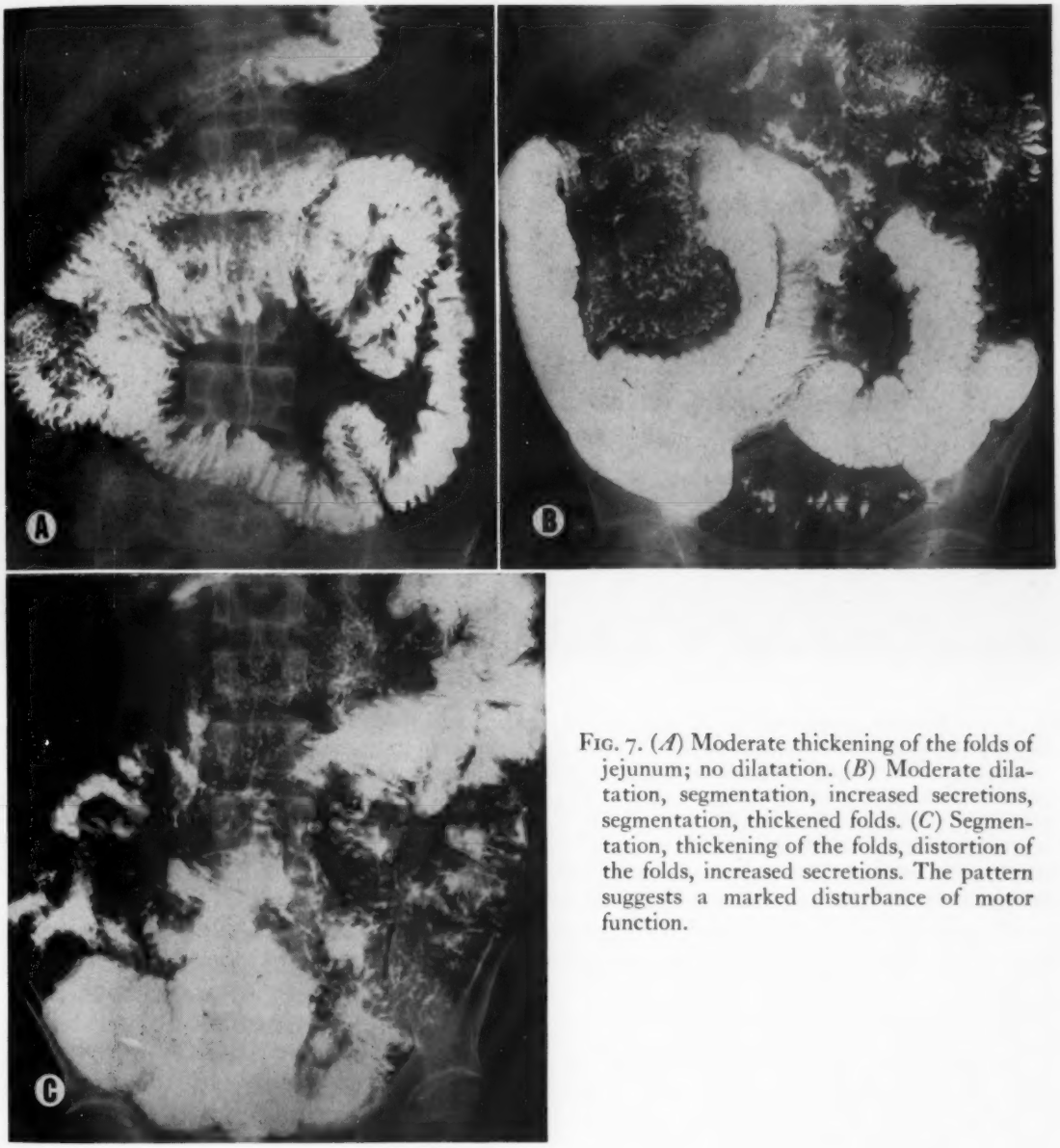

FIG. 7. (*A*) Moderate thickening of the folds of jejunum; no dilatation. (*B*) Moderate dilatation, segmentation, increased secretions, segmentation, thickened folds. (*C*) Segmentation, thickening of the folds, distortion of the folds, increased secretions. The pattern suggests a marked disturbance of motor function.

EFFECT OF THERAPY ON THE ROENTGEN APPEARANCE OF THE SMALL INTESTINE

Seventeen patients in this series have been maintained on liver therapy, vitamin B_{12} or folic acid. Twenty-two patients in this series have been treated with ACTH, cortisone or compound F, in addition to antianemic therapy to which they failed to respond. Four patients who had been treated for many years with liver extract have been in remission for periods of two to five years requiring no therapy ("arrested sprue"). However, moderate restriction of fat is still necessary to prevent flare-ups in these patients. One patient fifteen years ago presented marked segmentation, increased secretions and dilatation (Fig. 9*A*). Six months following liver therapy, the roentgen pattern was markedly improved (Fig. 9*B*). Two years later, it returned to normal. At the present time,

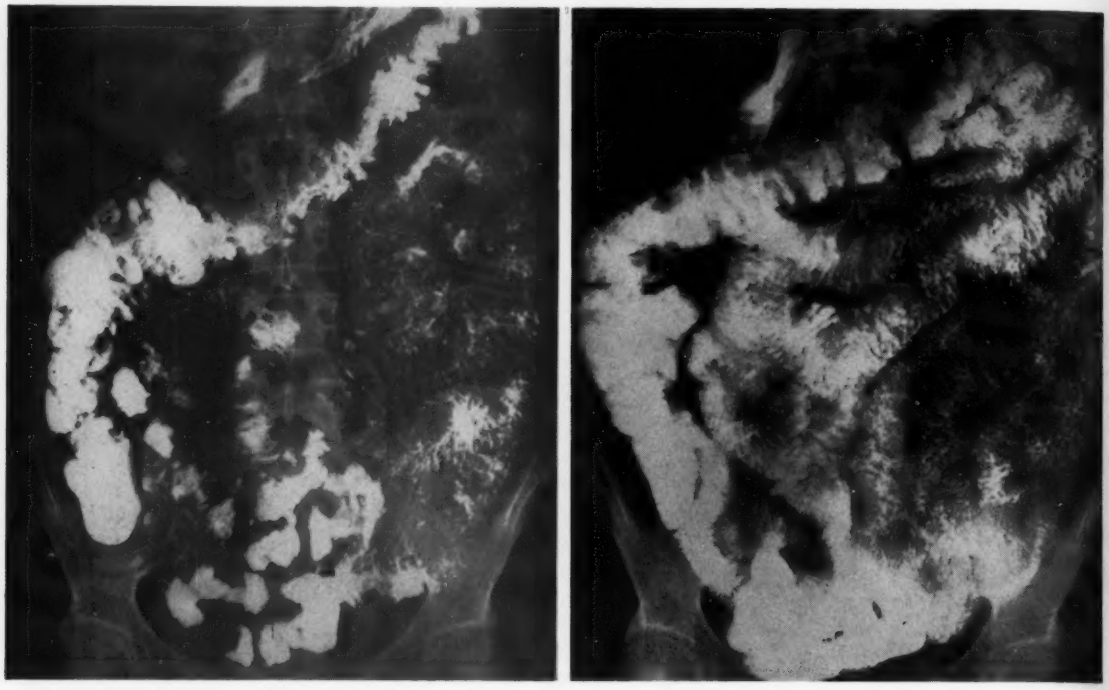

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FIG. 8. (*A*) Marked hypermotility. Barium column reached transverse colon in thirty minutes. Delayed segmentation, slight increased secretions. (*B*) After three months of cortisone, the small intestine appears within normal limits. There is still hypermotility, taking one hour to reach the colon.

the roentgen examination reveals a normal small intestinal pattern. The other 3 patients also show a normal small intestine at the present time. The original films in these 3 patients are unavailable for comparison.

Fourteen patients treated with antianemic preparations revealed insignificant or no changes following prolonged courses of therapy. The clinical results of adrenocortical therapy in patients resistant to other forms of therapy have been previously reported.[3] There is a considerable gain in weight, improvement of appetite and marked diminution in diarrhea and steatorrhea. The effects of this form of therapy on the sprue pattern have not been proportionate to the clinical improvement except in 2 patients in whom there was definite improvement with diminution of dilatation, secretions and the degree of segmentation (Fig. 4*A*, *B* and *C*). This occurred after two to four months of therapy. In 2 other patients, there was a reduction in segmentation and hypersecretion, but the dilatation persisted. Roentgen study of the small intestine will be continued to determine if there is any long-term improvement in the appearance of the small intestine following adrenocortical therapy.

Roentgen interpretation of improvement must be judged carefully because the roentgen findings vary from film to film and may even vary during the course of a single examination. Although in most patients there is a marked disrepancy between the degree of clinical improvement under therapy and the paucity of roentgen changes, in a few instances the improvement in the sprue pattern was significant.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis should be made between sprue and certain organic diseases of the small intestine, such as ileojejunitis. lymphosarcoma, tuberculosis, scleroderma,

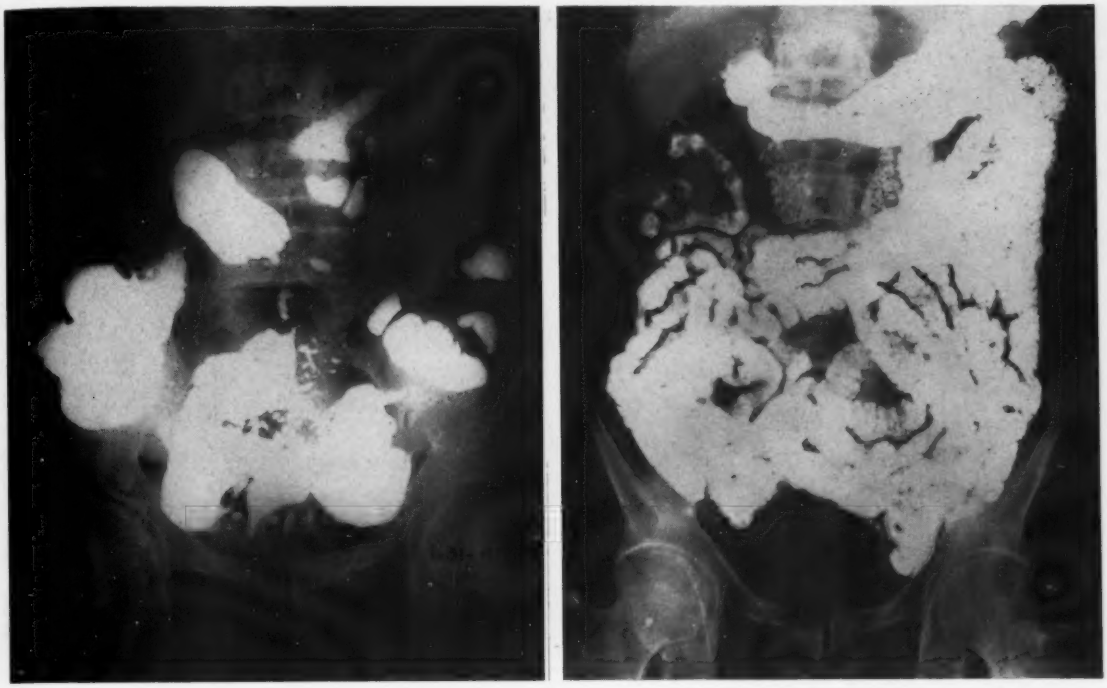

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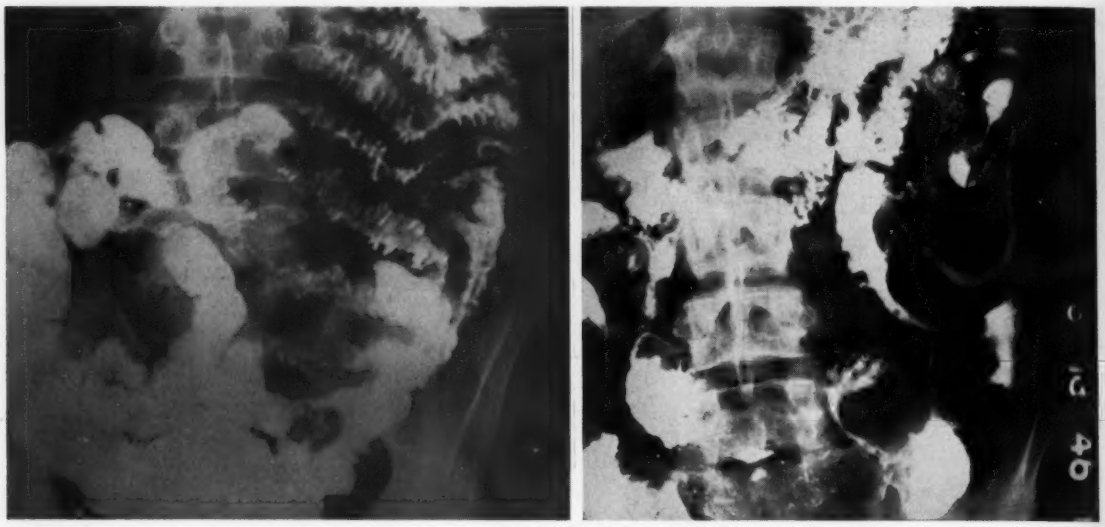
Fig. 9. (*A*) Immediate marked segmentation, increased secretions, moulage sign. (*B*) Six months after antianemic therapy, normal small intestine.

and amyloidosis, as well as those conditions that have been reported as producing, on occasion, a sprue-like pattern, namely, nephrosis, cirrhosis, hypoproteinemia, allergy, hyperthyroidism, parasitic disease, pellagra, anaphylactoid purpura, and other vitamin deficiency states.

Ileojejunitis. The literature states that, on occasion, the early roentgen changes of ileojejunitis are indistinguishable from sprue.[11,26] Inflammatory changes in sprue may occur, but are minimal in degree and extent as compared to the more characteristic changes of ileojejunitis. Inflammatory changes in ileojejunitis occur early and are intense. There is marked rigidity of the folds and lack of distensibility of the lumen of the intestine (Fig. 10*A*). Segmentation is not noted. Separation of the loops of intestine, secondary to the marked inflammatory reaction in the submucosa and in the mesentery, occurs early. The lack of response to medication is the usual finding in ileojejunitis. Neither the administration of antianemic or adrenal cortical medication nor the utilization of drugs that affect the autonomic nervous system, such as prostigmine or banthine, have served to modify the roentgen appearance of the intestine in ileojejunitis. We have not observed segmentation or the type of increased secretions seen in sprue, even in severe cases of ileojejunitis. Dilatation occurs only secondary to marked constriction of the rigid segments of intestine[24] (Fig. 10*B*).

Tuberculosis. Our experience with tuberculosis of the small intestine has been limited. Generally, the findings reflect marked inflammatory changes with rigidity and deep ulceration rather than the disordered motor pattern, segmentation and dilatation in the sprue pattern. Tuberculous peritonitis may produce dilatation, segmentation and increased secretions; however, areas of deformity with angulation are also noted, as well as inflammatory changes reflected in the mucosal pattern. The intestine in these



A *B*

FIG. 10. (*A*) The folds are thickened, blunted and in some areas, fused. The contour is irregular. There is rigidity and separation of the loops of intestine. The loops of intestine appear straightened, uncoiled. Diagnosis: nonstenotic form of ileojejunitis. (*B*) Entire small intestine is involved with alternating areas of constriction and dilatation. There is separation of the loops of intestine. The mucosal pattern in some areas is cast like; in another, it is reticulated. The loops of intestine appear to surround masses. Diagnosis: stenotic phase of ileojejunitis.

cases may return to normal after a course of streptomycin. Marked dilatation, increased secretions and evidence of disordered motor function are usually not seen.

Lymphosarcoma. Most cases of lymphosarcoma do not offer any difficulty in differential diagnosis. Filling defects produced by the tumor serve to identify the lesion, or the presence of pressure defects may be diagnostic. Dilatation at the site of the tumor with thickened folds may also be present. Areas of constriction with destruction of folds mimicking carcinoma have been seen, as well as fistula formation. The presence of extraluminal barium secondary to deep ulceration of the tumor has also been observed. In 2 patients, however, there was marked immediate segmentation, with dilatation and thickening of the folds (Fig. 11*A*). Both these patients had the classical findings of the sprue syndrome. An initial diagnosis of sprue was made; however, despite adequate therapy for sprue, they pursued a gradually retrogressive course. Autopsy revealed extensive lymphosarcoma.

A differential diagnosis at the onset of the illness between primary and secondary sprue can be extremely difficult. It may be of significance that the pattern in both these cases simulated one of the variants, rather than the characteristic pattern of marked immediate dilatation and secondary delayed segmentation.

Vagotomy and Gastrectomy. Several patients were observed who presented a roentgen appearance of marked paralytic ileus following vagotomy or subtotal gastrectomy with vagotomy. After the administration of barium, marked dilatation of the loops of intestine, especially the jejunum, was noted, followed by some delayed segmentation. Evidence of a disordered motor function, however, such as the linear and spotty scattering with the unusual amount of secretions, was not present. The findings also are temporary after the vagotomy and eventually disappear; the history is significant. A sprue-like pattern has been observed subsequent to subtotal gastrectomy.[13] Study of a large group of patients following subtotal gastrectomy would seem

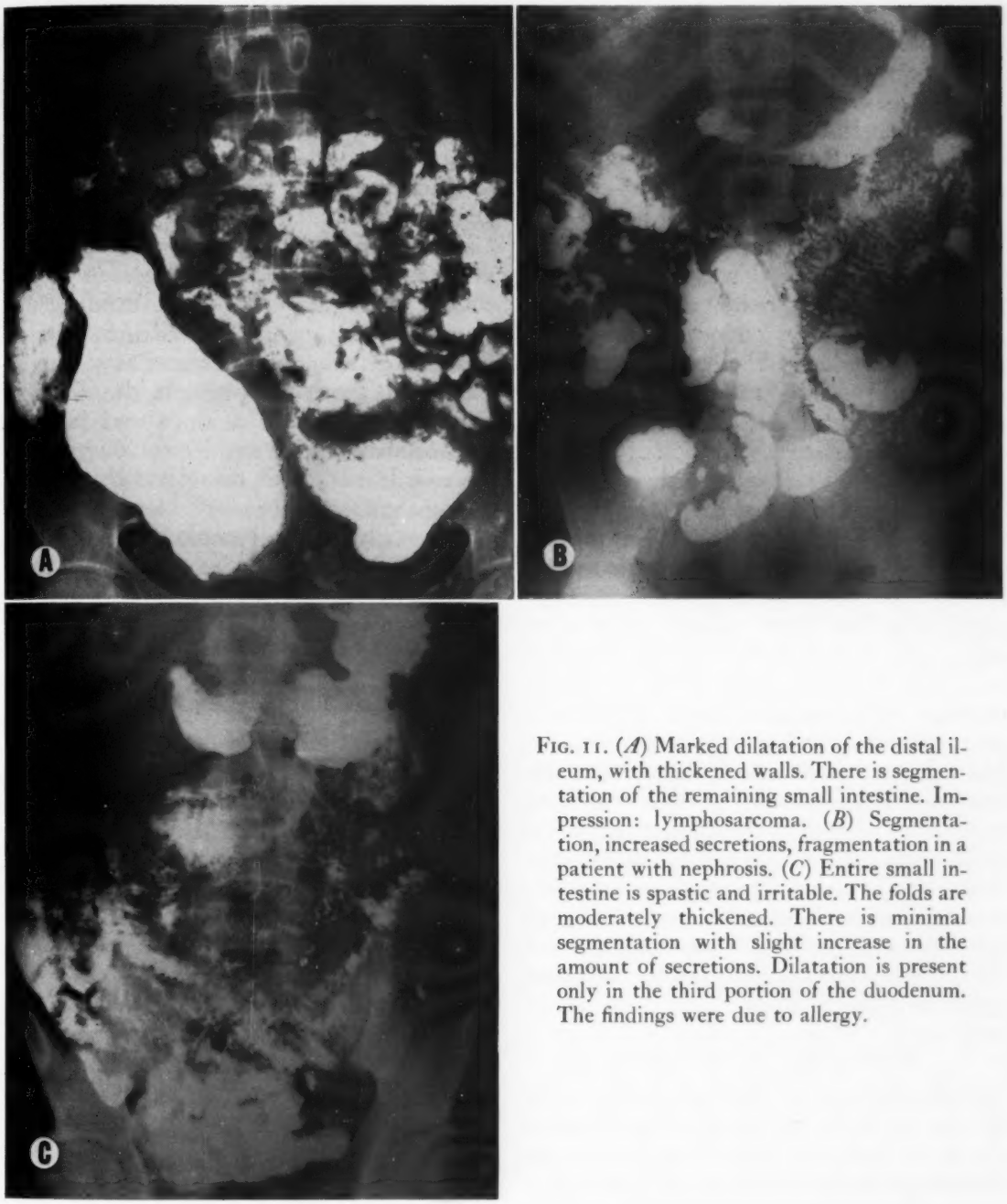


Fig. 11. (*A*) Marked dilatation of the distal ileum, with thickened walls. There is segmentation of the remaining small intestine. Impression: lymphosarcoma. (*B*) Segmentation, increased secretions, fragmentation in a patient with nephrosis. (*C*) Entire small intestine is spastic and irritable. The folds are moderately thickened. There is minimal segmentation with slight increase in the amount of secretions. Dilatation is present only in the third portion of the duodenum. The findings were due to allergy.

to indicate that this is an unusual complication.

Amyloidosis may involve the gastrointestinal tract, either primarily or secondarily. The 2 cases of primary amyloidosis that have been observed did not reveal evidence of the characteristic sprue pattern. In 1 case of secondary amyloidosis, immediate segmentation, increased secretions and slight dilatation, simulating one of the variants, were noted. Recently, several cases of amyloidosis of the small intestine have been reported.

Scleroderma. Several cases were studied with involvement of the small intestine. There may be moderate to marked dilata-

tion with hypomotility and marked atonicity of various segments of the small intestine. Segmentation, increased secretions, and fragmentation are not seen. Examination of the esophagus in these cases usually revealed a typical disturbance and was suggestive of the diagnosis.

There remain a large group of cases, such as nephrosis (Fig. 11*B*), cirrhosis, hypoproteinemia, allergy, pancreatic disease, pellagra, anaphylactoid purpura, Whipple's disease, which can, on occasion, produce a pattern similar to the sprue pattern described above. In most instances, the changes are not so striking as seen in the sprue pattern. Also, a variation of the sprue pattern is noted rather than the characteristic findings of marked dilatation and delayed segmentation and evidence of disordered motor function. Differentiation, on occasion, may be impossible. Allergy, especially, has been noted to produce changes very similar to sprue. Usually, however, there has been more irritability of the small intestine in allergy (Fig. 11*A*), and dilatation, followed by segmentation, has not been as marked. Removal of the offending substance may produce a striking reversal to normal in the appearance of the small intestine. Any chronic disease, particularly when associated with pyrexia and cachexia, may cause malnutrition of such severity as to produce a roentgen appearance that may be confused on occasion with the sprue pattern.

PATHOLOGIC OBSERVATIONS

Striking anatomic changes, which could be the basis for the disturbed intestinal function, have not been commonly observed either in tropical or nontropical sprue. The findings usually consist in thinning and atrophy of the wall with dilatation and distention of the small and large intestine. These changes, however, are minimal as compared to the roentgen findings.

Nevertheless, interesting findings have been reported.[2] The appearance of the mucosal surface of the small intestine may occasionally be more velvety than normal. On microscopic study, remarkable lesions consisting of hyaline bands and deformities of the villi (clubbing, mushrooming) were found. The implications of such lesions as a cause of the disturbance in the transport of nutrients across the intestinal membrane are obvious.

Large amounts of a granular pigment identified as hemofuscin were seen in the tunica mucularis of the gastrointestinal tract, especially in the small intestine. It was thought that this pigment may well be related to the ceroid pigment, described in vitamin E deficient animals and in man with malabsorption syndromes. Hypovitaminosis E might well round out the picture of deficiency of all fat-soluble vitamins in sprue, such as hypovitaminosis A (clinical and chemical evidence), deficiency of vitamin D (abnormalities of calcium metabolism and osseous changes) and of vitamin K (hypoprothrombinemia and bleeding).

Specific alterations in the myenteric plexus have been described.[15] However, in our cases, the submucosa and muscularis mucosae of the thinned small intestine were found to be intact and the plexuses of Auerbach and Meissner presented no alteration in their structure. The "neurogenic" etiology of sprue appears to be as questionable as some of the other theories. Many older pathologic observations in sprue must be discarded because they represent artefacts caused by autolysis. The small intestine is very susceptible to autolytic change and the relatively delicate hyaline lesions described above were particularly subject to change.

CLINICAL FINDINGS

The basic etiology of sprue is unknown, although a number of theories have been proposed.[23,27] At present, the concept prevails that sprue is a deficiency syndrome, causing or caused by disturbed intestinal absorption.[9,19,20,28]

The efficacy of a high protein diet and the response to therapy consisting of liver

extract, vitamin B_{12} and folic acid are compatible with the concept of a deficiency of dietary factors, the exact nature of which is unknown.

SYMPTOMS AND SIGNS

The chief symptoms of sprue are diarrhea and steatorrhea: bulky, tan-colored stools containing large amounts of undigested fat. In association with steatorrhea, there develops loss of weight which may be considerable, anemia usuallymacrocytic resembling the Addisonian type, and characteristic lesions of the mouth and tongue.

There are other associated abnormalities which are important from the diagnostic and therapeutic viewpoint, but are secondary to the disturbed function of the intestine and to defective absorption.[1] In severe cases of sprue, diminished concentration of calcium in the blood in association with tetany may be observed. Severe hemorrhage may develop as a result of malabsorption of vitamin K and hypoprothrombinemia. In some instances, pigmentation of the skin may be found and severe cases of sprue may resemble Addison's disease. Severe hypoproteinemia may develop with the associated signs of edema, ascites and hydrothorax.

During the active stage, almost all patients with sprue exhibit polyvalent vitamin deficiencies. The lesions of tongue and mouth are evidence of deficiency of the vitamin B complex factors, probably in combination with protein deficiency, but evidence of the lack of vitamins A, D, E, K, as well as of ascorbic acid, may be present. Thus, sprue may be associated with scurvy, osteoporosis, hypoprothrombinemia and pellagra-like symptoms. There may be evidence of hepatic damage, and cases of sprue with icterus, laboratory evidence of hepatic impairment and characteristic changes in the liver have been observed.[1]

The classification of the sprue syndrome into tropical and nontropical sprue, idiopathic steatorrhea, and celiac disease may be maintained for clinical purposes. The consensus favors the view that these conditions are varieties of the same disorder, the sprue syndrome.

The diagnostic criteria and the differentiation of "primary" and "secondary" sprue have been elaborated upon by many investigators.[1,3] A flat glucose tolerance test, flat vitamin A tolerance, low serum carotene levels and high concentrations of fecal fat, especially of fatty acids, are of great diagnostic significance, particularly in atypical or milder cases. There are rare instances of sprue without diarrhea in which formed, tan-colored stools contain large amounts of undigested fat. The mild and atypical cases may escape diagnosis for many years. Typical cases of sprue were observed in patients who had never left the temperate zone.

The diagnosis of "primary" sprue was established in this group of patients by the presently accepted criteria. Six of the patients were Puerto Ricans. Some of them probably developed their symptoms while living in a tropical climate and may represent the tropical variety of sprue. The remainder were considered to be instances of nontropical sprue.

The history revealed at some time all or most of the typical features of this syndrome. The most commonly observed physical findings were: evidence of marked weight loss, oral lesions, often painful, and abdominal distention; less often, clubbing of the digits and pigmentation were seen. The diagnosis was confirmed by characteristic results of multiple laboratory examinations. These included studies of the peripheral blood and bone marrow, chemical analyses of the serum for proteins, calcium and phosphorus, gastric analysis, pancreatic and liver function studies, prothrombin time determinations, glucose and vitamin A tolerance tests, roentgenologic examinations of the gastrointestinal tract and skeleton, stool cultures, stool examination for occult blood, ova and parasites, microscopic estimation of the stool for fat and

quantitative determinations of fecal fat content and fecal fat partition.

This series of 40 patients consisted of 30 females between the ages of twenty-six and seventy-five, and 10 males thirty-six to sixty-seven years of age. The age of onset of symptoms ranged from fourteen to sixty-nine years. However, there was often a history of vague but suggestive symptoms many years prior to the appearance of definite clinical manifestations.

Weight loss varied from 11 to 95 pounds. Diarrhea was present in varying severity in all but one patient who, however, did have definite steatorrhea. Glossitis and/or stomatitis was present in 28 patients, while abdominal distention was noted in 33 patients.

The hematologic data did not reflect the severity of the characteristic abnormalities usually seen during the natural course of this disease since many patients came under our observation while receiving various forms of antianemic therapy. Nevertheless, most of them had an anemia of varying degrees. Macrocytosis was often found whenever there was a marked anemia.

Bone marrow aspiration was performed in 16 of the 40 patients. Four had megaloblastic arrest. One patient had a hypoplastic marrow and 1 patient had findings consistent with an iron deficiency. The 10 patients who had normal findings were receiving antianemic therapy prior to this examination.

Serum proteins were determined in 33 patients. In 11, the concentration was less than 5 gm. per 100 milliliters and in 12 instances less than 6 gm. per 100 ml. The albumin concentration was found to be less than 2.5 gm. per 100 ml. in 6 and between 2.5–3 gm. per 100 ml. in 8 patients. Serum calcium was determined in 33 patients; in 22, it was found to be below 9 mg. per 100 ml. and in 5 between 9–9.5 mg. per 100 ml.

Steatorrhea was present in all patients. Quantitative determinations of fecal fat were performed in 24 patients, microscopic estimation of excessive amounts of neutral fats, fatty acids and soaps in 8, and in 5 only gross inspection of the stool was done. Fecal fat content represented 25 per cent or more of the dry stool weight in 21 patients. In the remaining 3, the values were 21.4, 23.5 and 21.9 per cent of dry fecal weight.

Vitamin A tolerance tests were performed in 25 patients. In 23 patients, the vitamin A absorption curve was flat, while in 4 there was evidence of delayed absorption. However, 3 of those patients had abnormally low fasting serum vitamin A levels. In 1 patient, the vitamin A tolerance curve was normal.

Serum carotene determinations were obtained in 24 patients and uniformly low levels were found.

Oral glucose tolerance tests were done in 35 patients. All but 1 showed evidence of impaired absorption. Thirty-two patients had typically flat absorption curves, while 2 showed moderate elevation of the blood level at the end of one hour.

Four patients with intestinal obstruction were observed. This complication was caused in 2 instances by volvulus of the sigmoid and in 1 instance by volvulus of the cecum; the nature of the obstruction could not be determined in the remaining patient at autopsy.

REPORT OF CASES

CASE 1. P. S., male, aged fifty-five, born in Poland, served with the Navy in World War I in Europe but was never in tropical countries. At the age of thirty-two, he began to complain of diarrhea with loose, foul, tan, greasy and frothy stools two to four per day. There were occasional exacerbations to fifteen to twenty stools in twenty-four hours. The diagnosis of sprue was established fourteen years after the onset of symptoms.

In July, 1948, he was admitted to Mt. Sinai Hospital because of extensive ecchymoses and hematomas over the lower half of his body. He appeared chronically ill with marked pallor and clubbing. The abdomen was distended. The prothrombin time was 128 seconds (control 12 seconds), hemoglobin was 9.9 gm. per 100 ml., platelet count 190,000. The oral glucose tolerance and vitamin A tolerance tests

were flat. The fasting vitamin A serum level was 32 micrograms (μg.) per 100 ml.; four hours and eight hours after ingestion of 180,000 units of vitamin A in oil the serum values were 37 and 34 μg. per 100 ml. respectively. The serum carotene was only 9 mcg. per 100 ml. Serum albumin was 3.9, globulin 1.4 per 100 ml., cholesterol 200 mg. and cholesterol esters 170 mg. per 100 ml. After large doses of vitamin K parenterally, the prothrombin time returned to normal values within three days. For the next three years (1948 to 1951) the patient was maintained on a low fat, high protein diet and received large doses of folic acid and vitamin B_{12}, at first parenterally and later orally. His stools averaged two to four a day and diarrhea was not a major problem. However, his weight remained between 110 and 115 pounds.

In May, 1951, the patient was readmitted to Mt. Sinai Hospital because of pain in the back, chiefly on walking. Physical examination revealed abdominal distention and decreased vibratory sense below the iliac crest bilaterally. The hemoglobin was 11 gm. and prothrombin time 12 seconds. Serum protein, calcium, phosphorus and electrolytes were normal. Stool examination revealed no ova or parasites and the guaiac test was repeatedly negative. Gastric analysis revealed free hydrochloric acid. Oral vitamin A tolerance and the oral glucose tolerance tests again showed flat curves, whereas the intravenous glucose tolerance test was normal. Pancreatic studies revealed a normal response to secretin. Roentgen survey of the bones disclosed moderate osteoporosis.

Barium meal examination revealed a normal esophagus, stomach and bulb. There was considerable dilatation of the entire jejunum, with a moderate amount of secretions. There was a moderate degree of dilatation of the remainder of the small intestine. The folds throughout the small intestine appeared to be thickened. Striking delayed segmentation and scattering were noted. On several of the films, huge, sausage-like loops filled with barium were observed. Between these loops, on occasion, there were noted the peculiar collapsed segments of intestine previously described (Fig. 1*B* and 2*B*).

The patient was started on a course of ACTH therapy and received 100 mg. daily in four divided doses. Improvement was striking; the number of stools dropped immediately to one formed stool a day. He gained 15 pounds in three weeks. ACTH was continued for four weeks with gradual reduction of the daily dosage to 50 mg. During the following nine months, oral cortisone was substituted for ACTH and the general improvement was fully maintained. However, barium meal examination done at this time revealed no essential change in the small intestinal pattern.

After cessation of cortisone therapy, there was definite evidence of relapse within four weeks. The diarrhea and steatorrhea reappeared, loss of appetite and loss of strength were noted and there was a gradual weight loss. In July, 1952, the patient was readmitted to the medical wards. The significant laboratory changes from the previous admission were as follows: serum albumin 2.8 gm. per 100 ml., serum cholesterol 95 mg. per 100 ml. The stool contained large amounts of fatty acids. The patient was treated with 60 mg. of hydrocortone daily. The diarrhea ceased and there was again marked objective improvement. In the subsequent months, this improvement was maintained with oral hydrocortone in doses of 20 mg. daily. His weight reached 125 pounds and he was able to resume full activities. A repeat roentgen examination of the small intestine failed to reveal any significant changes in his "sprue" pattern.

CASE II. C. S., male, Canadian, aged thirty-six, noted the gradual onset of cramp-like lower abdominal pain associated with four to six foul-smelling, bulky, semiformed stools daily two years previously.

He was treated in another hospital with parenteral liver extract, vitamins and a high protein, low fat diet. One month later, he had an episode of profuse bright red rectal bleeding, which required five transfusions. Shortly after he was admitted to the medical wards of Mt. Sinai Hospital because of a weight loss of 45 pounds.

Physical examination showed a chronically ill man in a poor nutritional state. Laboratory examination disclosed hemoglobin 11 gm., red blood cell count 3,830,000, white blood cell count 9,400, and a mild macrocytosis. The bone marrow was normal. Stool examination revealed large amounts of fatty acid crystals and some neutral fat. There were no ova or parasites and no pathogenic organisms were found on culture; guaiac test was 1 plus. The erythrocyte sedimentation rate was 20 mm. per hour (Westergren). Serum albumin was 3.0, serum globulin 2.7 gm. per 100 ml., calcium 9.2 mg., phosphorus

2.0 mg. per cent, and alkaline phosphates 12 King-Armstrong units; total cholesterol 143, cholesterol esters 106, phospholipid 189 mg. per 100 ml. Serum electrolytes were normal. The oral glucose tolerance test revealed a flat absorption curve, but the intravenous glucose curve showed a normal pattern. The vitamin A tolerance test revealed a flat absorption curve; the values at 0, 4, 6 and 8 hours were 31, 35, 31, and 28 μg. per 100 ml., respectively. The fasting serum carotene was 58 μg. per 100 ml. Pancreatic secretion studies were normal. Total fecal fat ranged from 33.5 to 46.1 per cent of the dry weight.

A barium meal examination revealed a normal esophagus and stomach. The folds in the second, third and fourth portions of the duodenum were thickened and slightly distorted. There was a moderate amount of increased secretions throughout the entire small intestine. Moderate dilatation of the jejunum was noted with marked delayed segmentation.

On a sprue diet supplemented with 20 mg. of folic acid daily and large doses of vitamin B, there was rapid improvement with disappearance of the diarrhea, abdominal cramps and distention. Because of the persistence of anemia, folic acid was injected in increasing amounts reaching a daily dose of 90 mg.; 10 μg. of vitamin B_{12} were added.

Eight weeks after discharge from the hospital, he was readmitted because of exacerbation of symptoms despite continuation of therapy. He had lost 14 pounds in nine days and had four to six light-colored watery stools per day. Repeated laboratory studies revealed no important changes. Intravenous ACTH followed by intramuscular injections of 100 gm. daily during the first week, 75 mg. during the second week and 50 mg. during the third and fourth weeks produced prompt and complete remission of symptoms. The diarrhea disappeared and he gained 42 lb. The most striking changes in the laboratory findings were the increase in serum albumin to 4.3 gm. per 100 ml. and a fall in total fecal fat to 11.5 per cent of dry stool. However, the oral glucose and vitamin A tolerance tests showed no significant changes.

Cessation of ACTH therapy caused a complete relapse in spite of the continued administration of antianemic therapy. Since August, 1951, the patient has been maintained on oral cortisone or hydrocortisone. His weight has reached 151 lb. Serum albumin remained in the range of 4.0 gm. per 100 ml. The fecal fat content remains within the normal range as long as an adequate dose of steroid compounds is prescribed.

Repeat roentgen examination of the small intestine revealed no change in the pattern described above.

CASE III. R. F., a Puerto Rican male, aged sixty-six, was first diagnosed as having tropical sprue in 1940. He was born in Puerto Rico and arrived in the United States in 1928. Progressive symptoms referable to sprue started in 1939 at the age of fifty-three. He developed weakness, anorexia, lost 29 lb. within six months and had an average of six to eight yellow watery stools per day. On his first admission in 1940, he appeared chronically ill, had a beefy, red tongue and some abdominal distention. There was also slight clubbing of the fingers and toes. Hemoglobin was 10 gm., red blood cell count 2.6 million with macrocytosis. Serum albumin was 4.5 gm. and globulin 1.7 gm. per 100 ml. Serum calcium as well as other electrolytes were normal. Serum cholesterol was 90 mg. per 100 ml. The oral glucose tolerance test showed a flat curve. Gastric analysis revealed free HCl.

Barium meal examination revealed a normal esophagus and stomach. The second, third and fourth portions of the duodenum were slightly dilated, with moderate thickening of the folds. There was immediate marked and persistent segmentation, with considerable secretions. The moulage sign was present in the segmented loops (Fig. 9*A*). A diagnosis of tropical sprue was made and the usual diet with supplements of vitamins and injections of liver extract were given. There was a rapid improvement in all symptoms.

Barium meal examination after six months of liver therapy revealed a normal small intestine; there was no evidence of segmentation, increased secretions or dilatation (Fig. 9*B*). In 1948, the injections of liver extract were discontinued and the patient showed no recurrence of symptoms. In September, 1950, he was readmitted for evaluation. The clinical and laboratory data were compatible with the diagnosis of sprue in full remission. The blood count was normal. The serum vitamin A level was 47 μg. per 100 ml. There was a normal rise after the administrations of a standard dose of vitamin A. The carotene level was 104 μg. per cent. Repeat roentgen examination disclosed a normal small intestinal pattern.

CASE IV. V. S., a white female, aged thirty-

two, whose case history was presented in detail in a previous publication (*Gastroenterology*, 1951, *19*, 674).

Since December, 1950, this patient, who was resistant to the accepted methods of sprue therapy, has been maintained on prolonged oral cortisone. Weight reached a peak of 110 lb. in May, 1951. The total fecal fat was repeatedly under 25 per cent of total dry weight, but increased as soon as cortisone therapy was reduced. All her abnormal laboratory findings reverted to normal.

Barium meal examination revealed a moderate degree of dilatation of the entire small intestine, slightly more marked in the distal jejunum. There were also moderate amounts of hypersecretion throughout the small intestine and moderate thickening of the folds in the distal jejunum. On the early roentgenograms there was slight segmentation. However, as the barium left the intestine, marked segmentation and fragmentation were noted (Fig. 4*A* and *B*). This pattern persisted for two years. Following the administration of cortisone slight segmentation and slight hypersecretion remained (Fig. 4*C*). The dilatation, "late" segmentation and thickened folds had completely disappeared.

Case v. E. P., white female, died at the age of thirty-three during her sixth hospital admission. The diagnosis of nontropical sprue had been established during previous admissions on the basis of diarrhea, steatorrhea, anemia, hypoproteinemia and hypocalcemia, free HCl in the gastric juice, normal pancreatic enzymes following secretin, flat oral glucose tolerance test curve and a flat vitamin A tolerance test curve.

The first admission was at the age of twenty-one in 1932 with chief complaints of weakness, weight loss and ankle edema. The anemia was microcytic and the serum A/G ratio was 3.6/1.6. Two subsequent admissions revealed a typical clinical picture of nontropical sprue. There was severe diarrhea and steatorrhea, serum albumin was 2.5 and globulin 1.5 per cent, serum calcium was 6.3 mg. per cent.

Barium meal examination revealed striking dilatation of the mid- and distal jejunum with moderate dilatation of the proximal jejunum (Fig. 2*A*). The folds were somewhat distorted and thickened. There was a slight amount of hypersecretion; "late" segmentation was noted, especially in the ileum.

Between 1932 and 1944, she was admitted to various institutions for persistence of the above symptoms and gradually developed cachexia. Prior to her last and final admission in 1944, she had lost 30 lb. in three months and weighed only 89 lb. Chief complaints were diarrhea with four to five loose, watery, light yellow stools, extreme weakness and ankle edema. On physical examination, she appeared chronically ill, with marked atrophy of the breasts, and there was no evidence of any subcutaneous fat. The finger tips were moderately clubbed, the abdomen was scaphoid. Hemoglobin was 14 gm., red blood cell count 4.7 million. The stool contained neutral fat in small amounts and abundant fatty acid crystals. Tests for occult blood were negative. Serum albumin was 2.5 gm. per 100 ml., serum globulin 1.5 gm. per 100 ml., calcium 8 mg. per 100 ml.; alkaline phosphatase was 31 King-Armstrong units. Repeat roentgen examinations revealed no change in the previously observed findings; dilatation continued to be the most pronounced roentgen characteristic. Various unsuccessful efforts to improve her nutrition were made; the patient's condition became progressively worse and she died within a month.

Autopsy revealed a high degree of steatosis of the liver, atrophy of all other viscera, a very slight distention of the intestine and thrombosis of the dural sinuses and cervical veins.

Case vi. C. H. The diagnosis of nontropical sprue was established in this white female, aged forty-six, in November, 1950. Symptoms started insidiously in 1949 and developed into marked diarrhea, six to twelve foul smelling, frothy, yellowish watery stools with rapid weight loss. Therapy consisted of repeated transfusions in addition to the usual sprue diet supplemented with vitamins and injection of liver extract.

In November, 1951, an exploratory laparotomy was performed in another hospital and revealed no organic disease of the gastrointestinal tract. Biopsies revealed nonspecific mesenteric lymphadenitis and fatty infiltration of the liver. On admission to Mt. Sinai Hospital in September, 1951, the patient appeared cachectic; moderate abdominal distention was present. Red blood cell count was 3.2 million, hemoglobin 10 gm. Bone marrow aspiration was reported as normal. Serum albumin was 3.2 gm., serum globulin 3.3 gm. per cent, serum calcium 9.1 mg. per cent. The stool contained large amounts of fatty acids. The gastric juice contained free acid. Pancreatic function after secre-

tion was normal. Oral glucose tolerance test revealed a flat curve, as did the vitamin A tolerance test. Fasting serum vitamin A was 14 μg. per cent and after a standard dose of vitamin A_{12}, 12 and 10 μg, were found at four, six, and nine hours, respectively. The carotene level was low, 7 μg. per cent.

Barium meal examination revealed a normal esophagus, stomach and bulb. There was marked hypermotility of the barium through the small intestine. The barium column reached the cecum in forty-five minutes (Fig. 8*A*). As the barium left the intestine, slight hypersecretion, slight segmentation and fragmentation were noted. Several repeat examinations during the same year revealed no change in the marked hypermotility or "late" segmentation. This patient had been maintained on parenteral vitamin B_{12} and liver therapy with marked, but not complete, remission. She was started on ACTH with rapid and remarkable improvement (Fig. 8*B*). During 1952–1953, ACTH therapy was continued in repeated courses, alternating with cortisone and hydrocortisone. Symptoms have been controlled with hormonal therapy. The total weight gain was 50 lb. and she has been able to resume her normal activities. Roentgen examination revealed less hypermotility and, at this time, the "late" segmentation, the hypersecretion and the slight fragmentation were absent.

DISCUSSION

Snell and Camp[26] were among the first to describe the roentgen pattern associated with "idiopathic steatorrhea." Their findings included delayed motility, changes in the mucosal relief pattern of the jejunum and obliteration of the markings of the valvulae conniventes. Clumping of barium and a loss of the sharply margined contour of the duodenum and proximal jejunum were also noted. Mackie, Miller and Rhoads[22] described thickening of the mucosal folds, irregular dilatation of the duodenum and proximal jejunum and the collection of short smooth segments of barium associated with spasm in the adjacent intestine. In the opinion of these groups of investigators, these changes were not typical of chronic idiopathic steatorrhea but might be seen in any diffuse inflammatory process of the small intestine. Golden[15] described the roentgen abnormalities of the small intestine associated with nutritional disturbance including changes in motility, tone, abnormal segmentation and dilatation. He suggested that the term "disordered motor function" of the small intestine be substituted for "deficiency pattern." Sussman and Wachtel[29] questioned the predominance of a neurogenic etiology for the abnormal roentgen pattern in sprue. These authors among others[5,12] reproduced a segmentation pattern following the introduction of fatty mixtures in the small intestine. In general, therefore, though most of the roentgen findings in sprue have been described, the specificity of the pattern has not been emphasized.

The studies made in this series of patients suggest that the roentgen appearance of the small intestine in sprue is sufficiently characteristic to be of diagnostic value in 70 per cent of the patients. This pattern consists of dilatation of the mid- and distal jejunum, "late" segmentation or flocculation, hypersecretion, thickening of the folds, scattering and evidence of disordered motor function. These roentgen changes do not occur in any other condition with the frequency or the character they exhibit in sprue, although they may, on occasion, be found to a lesser degree in nephrosis, parenchymatous liver disease, pancreatic steatorrhea, allergic purpura, hyperthyroidism, hookworm disease, pellagra, and other nutritional deficiency states. The absence of inflammatory changes in the roentgen pattern in sprue is also characteristic and serves to distinguish it from ileojejunitis, tuberculosis and other inflammatory diseases of the small intestine. In 4 patients in this group, a roentgen pattern was observed, characterized by marked, "early," and persistent segmentation, hypersecretion and moderate dilatation. This is the pattern that has been frequently described in sprue. Also, it is this pattern that has been seen more commonly in secondary sprue as well as in those conditions that have been mentioned above and described as "deficiency pattern," "en-

teropathy in deficiency states," "irritation pattern," "disordered motor function," etc. The inclusion of so many different diseases and disorders, often because of the presence of one roentgen variation, has caused such a dilution of the term "deficiency pattern" that it has lost its meaning. It appears preferable that when the roentgen findings in the small intestine are solitary and isolated, an all-inclusive term such as "pattern" should be avoided and a descriptive report alone should be made by the roentgenologist.

The roentgen diagnosis of "sprue pattern" should be reserved for the severe alterations observed in the majority of patients with sprue as described above.

SUMMARY

Forty patients with sprue have been studied clinically and roentgenologically over a period of one to seventeen years; three patients more than fifteen years, eight more than five years, twenty more than three years and ten, one year or less. The chief symptoms and signs included steatorrhea, weight loss, anemia, oral lesions, hypocalcemia, hypoproteinemia, flat vitamin A and glucose tolerance curves and normal pancreatic enzyme studies. These patients were observed roentgenologically prior to and following treatment in the hospital, though the vast majority had received some form of antianemic therapy before coming under our control.

Three patients revealed a normal small intestinal pattern. The remainder exhibited two distinctive patterns. The first and most characteristic was observed in 70 per cent of the patients in this series and consists of dilatation most prominent in the mid- and distal jejunum, segmentation, large 4–10 cm. long barium-filled loops of ileum best visualized during the evacuation of the barium meal, thickening of the mucosal folds and the presence of hypersecretion of an altered quality. While each of these features may occur in a wide variety of disorders, they are more frequent in and more pronounced in sprue. In the second pattern, segmentation is marked, early and persistent and present throughout the small intestine, secretions are pronounced and dilatation is slight to moderate. This latter pattern occurred in only 10 per cent of the patients in this series and is also observed on occasion in those conditions and diseases simulating sprue; namely, nephrosis, hyperthyroidism, cirrhosis, pancreatic steatorrhea, pellagra and other deficiency states.

Differential diagnosis must also include organic diseases of the small intestine, including lymphosarcoma, ileojejunitis, tuberculosis, amyloidosis and scleroderma.

Roentgen evidence of improvement in the sprue pattern was significant in three patients following steroid therapy to the present time and in four patients who have been treated for many years with antianemic therapy.

The "sprue pattern" is sufficiently distinctive roentgenologically to separate it from the heterogeneous group of conditions heretofore labeled with the roentgen diagnosis of "irritation pattern," "enteropathy in deficiency states," "deficiency pattern," or "disordered motor function."*

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VOL. 72, NO. 3

AMYLOIDOSIS OF THE SMALL INTESTINE*

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AMYLOID is a protein material which exhibits certain chemical reactions resembling those of starch. Amyloidosis is the term applied to the presence of this substance in various organs or tissues in the human body.

Amyloidosis is usually divided into two groups, primary and secondary. In the latter, the deposits of amyloid occur in association with other diseases, such as chronic infections, leukemia, Hodgkin's disease, myeloma, etc. Primary amyloidosis occurs without association with other diseases; its cause has not been determined. In either primary or secondary amyloidosis, fatal interference with some vital function occurs eventually.

The purpose of this paper is to present 3 cases of amyloidosis in which striking abnormalities of the small intestine were demonstrated by roentgen methods of examination.

LITERATURE

Dahlin (1949) reported 30 cases of secondary amyloidosis with involvement of various organs, particularly the liver and kidneys; other organs were involved less frequently, including the gastrointestinal tract. Dahlin also reported 8 cases of primary amyloidosis, with involvement of the gastrointestinal tract in all of them.

In 1933 Randall described a case of myeloma complicated by amyloidosis of the intestine with gas distention interpreted as evidence of intestinal obstruction. At operation no obstruction was found. The small intestine was dilated and its wall was greatly thickened and contained whitish deposits. At necropsy the small intestine was larger than the colon. Large amounts of amyloid were found in the tunica muscularis of the small intestine, more in the circular than in the longitudinal muscle coat, but none was found in the mucosa or in other organs.

Koletsky and Stecher (1939) reported a case in which the longitudinal layer of the tunica muscularis of the small intestine was interrupted by nodular masses of amyloid, none of which was found in the circular layer. The muscularis mucosae was irregularly replaced by this substance. These writers reviewed 23 cases of primary amyloidosis found in the literature. In 8 cases amyloid was found in the intestine, and the associated symptoms included constipation, diarrhea, abdominal pain, vomiting and "meteorism." Intestinal bleeding occurred in 3 cases, in 2 of which it was the cause of death. Ileus was given as the cause of death in 2 cases.

Pearson, Rice and Dickens (1941) reported 2 cases of primary amyloidosis. In 1 of them the esophagus, stomach and small intestine, as well as other structures, were involved. Massive infiltration of amyloid in the tunica muscularis of the jejunum and ileum, with patchy areas in the mucosa, was found. The walls of the small intestine averaged 0.5 cm. in thickness. The submucosa of the esophagus, stomach and small intestine appeared as an irregular band of amyloid.

Gerstel (1932) reported a case with amyloid in the wall of both small and large intestine. A portion of the small intestine 80 cm. in length had thick walls and resembled a stiff tube. The mucosa was absent and was replaced by a layer of granulation tissue covering the amyloid-containing muscularis mucosae.

Gottron (1932) reported a case of amyloidosis with abdominal distention resembling ileus and with involvement of the skin giving a scleroderma-like picture. The pas-

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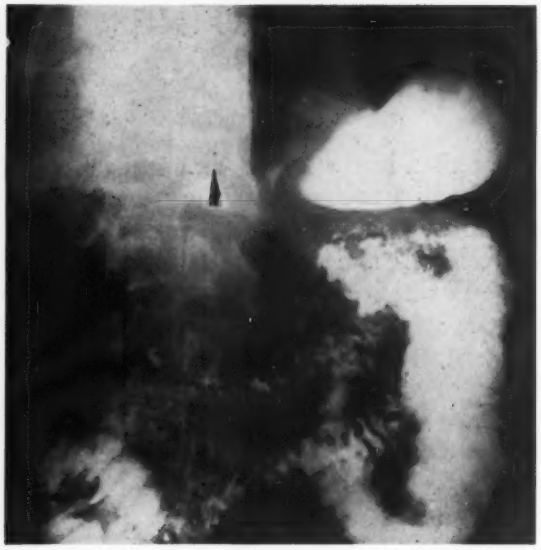

FIG. 1*A*. Case 1. Amyloidosis of the small intestine with gas distention simulating ileus. The mucosal folds of the jejunum are irregularly widened. Compare with Figure 1*C*.

sage of barium through the intestine required five days.

These reports, taken more or less at random from the literature, show that the small intestine is frequently the site of amyloid deposits, as are also the esophagus, stomach and large intestine. Any one, or all of the layers of the wall may be involved in various degrees. The replacement of muscle is sometimes associated with gas distention, resembling ileus, for which it may be mistaken.

CASE REPORT

Three case reports are given to illustrate the problems in differential diagnosis which may be encountered in the examination of patients with amyloidosis who have abdominal symptoms.

For Case 1, I am indebted to Dr. R. A. Powers, Palo Alto, California, and to Dr. R. R. Newell, San Francisco, California. This was published in "Radiologic Examination of the Small Intestine" (Lippincott, Philadelphia, 1945).

CASE 1. A man, aged sixty, was admitted to the Palo Alto Hospital May 15, 1942, because of pain in the shoulder of about eight months' duration and pain in the epigastrium of five weeks' duration. Roentgen examination disclosed dilatation of the upper part of the small intestine and coarsening of the mucosal folds of certain loops of jejunum (Fig. 1*A* and *B*). A moderate secondary anemia was present. The stools contained a small amount of fat. The abdomen became distended and the clinical picture suggested intestinal obstruction. At operation dilatation of the upper two-thirds of the small intestine was found. The wall was thickened and edematous, with a granular serosal surface. A biopsy from the intestinal wall disclosed amyloidosis. He died thirty-nine days after operation. At necropsy the entire jejunum and proximal ileum were distended, with small whitish translucent nodules and strips in the serosa. Microscopic examination disclosed abundant deposits of amyloid between the muscle bundles of the tunica muscularis and the muscularis mucosae. It was present in the mucous membrane, in the walls of the blood vessels of the submucosa and in the nerve ganglia of the submucosal plexus (Fig. 1*C* and *D*). Little or none was found in the stomach and large intestine. This case is to be classed as primary amyloidosis.

FIG. 1*B*. Case 1. Gas distended loops of small intestine with thick walls lie in the right flank on a film taken after a barium enema.

Case II. A man, aged forty-two (Unit No. 048643), came to the Presbyterian Hospital on May 24, 1951, complaining of difficulty in closing the right hand of two years' duration, for which he had a scalenus operation one year previously without improvement. He also complained of difficulty in moving the right shoulder for eight months. During the 1930s he had been a heavy drinker. Albuminuria was discovered in 1942 and had persisted. The urea nitrogen was 17 in September, 1950 and rose to 39 in April, 1951. Because of persistent vomiting, roentgen examination of the gastrointestinal tract was done elsewhere on April 12, 1951, about six weeks before he came to the Presbyterian Hospital. This disclosed an apparently normal mucosal pattern in the jejunum with extremely slow movement of the barium through the small intestine. In six hours it had not progressed beyond the middle of the jejunum (Fig. 2*A*). No gas distention was present. A film of the right shoulder May 29, 1951, showed definite evidence of a slight subluxation of the head of the humerus from the glenoid. Films of the hands on May 29, 1951, disclosed no bone abnormality. After admission on June 5, 1951, a film of the abdomen was taken because of vomiting and colicky epigastric pain,

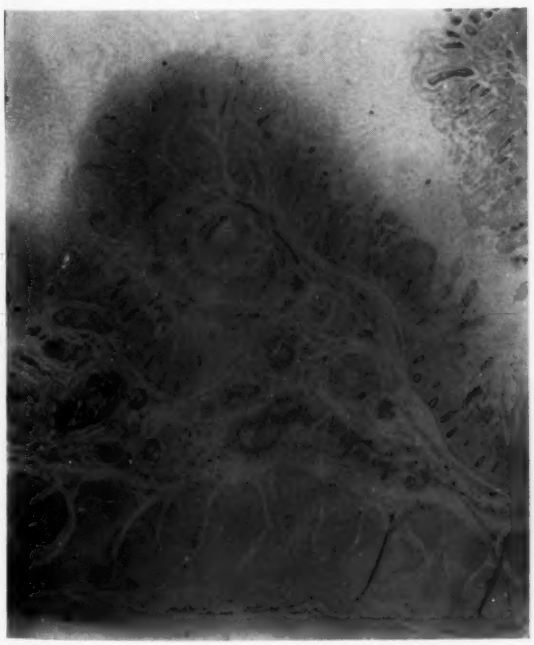

Fig. 1*C*. Case 1. A low power photomicrograph showing the wall of the jejunum with a mucosal fold greatly thickened by amyloid.

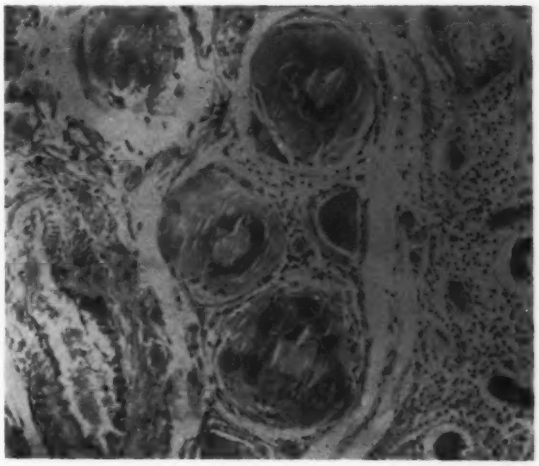

Fig. 1*D*. Case 1. A high power photomicrograph shows submucosal ganglia in which the nerve cells are largely replaced by amyloid.

which showed "mild gas distention of the small intestine compatible with early small bowel obstruction." The blood count was normal. The blood protein was 5.9, albumin 3.9. Under a strict low salt regimen the urea nitrogen fell from 70 to 24. Later it rose to 41. The blood calcium, phosphorus, sodium and potassium were normal. On June 17, 1951, he had an attack of cramping upper abdominal pain and diarrhea, but on June 19 he was allowed to go home because he seemed to be feeling better. On July 24 he was readmitted because of increasing weakness and vomiting without nausea. At this time the erythrocyte sedimentation rate was 45. The nonprotein nitrogen was 77. The abdomen was moderately distended. The possibility of a collagen disease was discussed by the clinicians. Barium enema on August 8, 1951, disclosed no obstruction or abnormality in the colon but the small intestine was dilated and distended with gas just as it was on the film of June 5, and the possibility of paralytic ileus was suggested (Fig. 2*B*). The nausea and vomiting persisted. Prostigmine in adequate doses had no effect on the distention. On August 23, 1951, a small intestine study was done which disclosed an extremely slow transit time (Fig. 2*C*). In twenty-four hours a large part of the opaque material remained in the jejunum. A film at forty-eight hours (Fig. 2*D*) showed a little barium in the large intestine but most of it remained in practically the entire length of the small intestine. As on previous films, the walls of the gas-distended loops of the jejunum

FIG. 2*A*. Case II. Amyloidosis of the small intestine with gas distention. The six hour film, April 12, 1951, shows that the opaque material had not progressed beyond the upper loops of jejunum. The loops appear hypotonic but the mucosal folds are not abnormal. No gas distention is present.

and ileum appeared abnormally thick. Urecholine was given for three days and produced no effect on the gas distention but did cause a diarrhea, presumably because of its effect on the large intestine.

The failure of the small intestine to respond to urecholine suggested some disease of the wall which made the parasympathetic chemical mediator (urecholine) ineffective; scleroderma and amyloidosis with replacement of muscle were mentioned as possibilities. Because of the thickness of the wall, it seemed that amyloidosis was the more likely. A biopsy of the gum disclosed the presence of amyloid. The patient died on October 23, 1951, because of increasing renal insufficiency, malnutrition, and pneumonitis.

At necropsy (No. 16677) primary amyloidosis was found involving the tongue, esophagus, gastrointestinal tract, heart, the capsule of the right shoulder, and many blood vessels. The tunica muscularis of the small intestine was almost completely replaced by amyloid, especially in the lower jejunum and upper ileum. The walls were tremendously thickened (Fig. 2*E*). The mucosa was atrophic but otherwise intact.

CASE III. A man, aged forty-four (Unit No. 944702), was admitted on March 2, 1949, because of loss of appetite, nausea, and constipation of three months' duration and a loss of 40 pounds in weight during the previous two years. The stools were positive for occult blood. The hemoglobin was 11 gm., red blood cell count 5.3 million, white blood cell count 21,100, polymorphonuclear leukocytes 87 per cent. The urine contained albumin and both red and white cells. Sigmoidoscopy March 18, 1949, disclosed a granular and friable mucosa which bled easily; this was interpreted as consistent with early ulcerative colitis although no ulcers could be seen. Intravenous urography March 31, 1949, disclosed enlargement of the kidneys with an abnormality of the upper calyx of the

FIG. 2*B*. Case II. The postevacuation film following a barium enema on August 8, 1951, shows to good advantage the gas distended loops of small intestine with thick walls. This appearance was demonstrated on films of the abdomen two months previously.

right kidney. Retrograde pyelography again disclosed "distortion" of the upper calyx of the right kidney, and elongated calyces which suggested polycystic disease.

A small intestine study, April 7, 1949, disclosed both narrowed and slightly widened loops of ileum. The margins of the narrowed loops were irregular and abnormal, suggesting mucosal destruction (Fig. 3*A*). The transit time was slow. The barium suspension reached the cecum in six hours, with the help of a food stimulus. The ten hour film (Fig. 3*B*) shows considerable barium remaining in the lower loops of the abnormal ileum, further evidence of hypomotility. No tenderness and no mass were found on palpation. The cecum was not abnormal. This was interpreted as regional enteritis.

On April 8, 1949, one of the internists suggested that the patient might have amyloidosis with regional enteritis. A biopsy of the gum, following prolonged study with special stains, was interpreted as showing evidence of amyloid. On April 15 the patient began to have fever, spiking up as high as 101°F. He insisted on leaving the hospital on April 16, but returned two days later because of abdominal cramps, and diarrhea, which persisted. Vagotomy was done on May 5, 1949, hoping to relieve the symptoms attributed to regional enteritis. The patient died on May 11, 1949.

Fig. 2*C*. Case 11. The one hour film of a small intestine study August 23, 1951, shows that the stomach is emptying satisfactorily. The upper loops of jejunum show some thick mucosal folds. Gas distended loops with thick walls can be seen distal to the barium shadows.

Fig. 2*D*. Case 11. Forty-eight hours (August 25 1951) after ingestion of barium (Fig. 2*C*), the opaque material was distributed throughout the small intestine. This is a striking demonstration of the disturbance in motor function resulting from replacement of muscle by amyloid.

Necropsy disclosed fibrinopurulent general peritonitis, for which no satisfactory explanation could be found. A clear cell carcinoma 9 cm. in diameter projected from the upper pole of the right kidney. The ileum appeared normal in width. Amyloidosis of the kidneys, liver, spleen, pancreas, adrenals, stomach, small intestine and colon was demonstrated. The mucosa of the ileum was atrophic and edematous. The villi were widened and reduced in height by irregular deposits of amyloid. The effect was to smooth the inner surface of the intestine. The muscularis mucosae was more involved than any other structure. The blood vessels of the submucosa and tunica propria contained patchy deposits of amyloid. The enlargement of the

FIG. 2*E*. Case II. A low power photomicrograph of a section of the intestinal wall shows the tremendous widening of the tunica muscularis due to replacement of muscle by amyloid. The mucosa is partly autolyzed. The muscularis mucosae is slightly thickened.

kidneys, which suggested polycystic disease, was the result of amyloidosis. Because of the carcinoma of the kidney, this case is presumably to be classed as secondary amyloidosis.

FIG. 3*A*. Case III. Amyloidosis of the small intestine simulating regional enteritis. A spot film taken about six hours after the ingestion of barium discloses irregular narrowing of the terminal ileum. The abnormal inner surface of these loops suggests mucosal destruction and was interpreted as regional enteritis.

FIG. 3*B*. Case III. A film taken ten hours after the ingestion of barium shows several loops of lower ileum still filled with barium, some of which are irregularly narrowed. At this time the normal ileum should have expelled its contents into the large intestine.

DISCUSSION

Amyloidosis produces a complex and confusing clinical picture, which cannot be

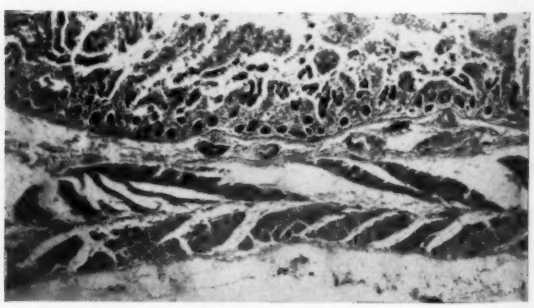

FIG. 3*C*. A low power photomicrograph of a section of the ileal wall shows evidence of atrophy of the mucosa, manifested by wide spacing of the glands. The amyloid was in the blood vessels of the tunica propria and the submucosa. Patches of it were found in the muscularis mucosae and the mucosa itself. The submucosa and the tunica muscularis are not widened. Some autolysis of the mucosa has occurred.

discussed here. Amyloid is deposited in different tissues in different individuals. For example, it may be extensively present in the tunica muscularis of the intestine with very little in the mucosa and submucosa in one person, or the opposite may occur in another. In many cases reported in the literature, gas distention of the intestine was mentioned as "meteorism," "ileus," or "obstruction." Abdominal symptoms were frequently present which were consistent with disease or serious disorder of the gastrointestinal tract.

In Case I, as in the case reported by Randall (1933), the clinical picture and the gas distention were so consistent with mechanical ileus that the abdomen was opened and the diagnosis of amyloidosis was made by biopsy of the intestine.

In Case II, the various roentgen examinations disclosed persistent gas distention of the small intestine over a period of more than ten weeks, and at first was thought to be suggestive of an unusual paralytic ileus for which no physiological explanation could be found, such as hypoproteinemia or hypopotassemia.

Failure of the intestine to respond to prostigmine indicates a lack of acetylcholine in the wall. This occurs with hypoproteinemia and hypopotassemia. However, in such cases, the muscle is still capable of responding to urecholine or other derivatives of acetylcholine (Golden, 1950). In Case II no response to urecholine could be detected in the small intestine over a period of three days, although the drug affected the large intestine sufficiently to cause diarrhea. This was thought to indicate the presence of some organic disease of the wall of the small intestine which prevented the muscle from reacting to the parasympathetic chemical mediator. Although rare, both scleroderma and amyloidosis were mentioned as possible explanations for these phenomena. Because of the thickness of the intestinal wall, amyloidosis was thought to be the more likely of the two. Furthermore, a deposit of amyloid in the muscle coat would explain not only the thickness of the shadow of the wall but also the gas distention and the failure to respond to the acetylcholine derivative. One of the internists noted slight enlargement of the tongue. These two observations lead to the biopsy of the gum and tongue which demonstrated the presence of amyloid.

The subluxation of the shoulder was explained at necropsy by the amyloid in the capsule. Koletsky and Stecher (1939) mentioned subluxation of a shoulder in a case of amyloidosis but gave no anatomical explanation for it. In Case I, pain in a shoulder was mentioned without further description.

In Case III, the amount of amyloid in the intestinal wall was small compared with that in Case II. It was mainly in the blood vessel walls of the tunica propria of the mucous membrane and of the submucosa. and to some extent in the muscularis mucosae. The abnormal margins of the barium shadows, which were interpreted as evidence of mucosal destruction, were probably the result of irregular atrophy and of irregular deposits of amyloid in the mucous membrane. Inasmuch as the ileum was normal in width at necropsy, the persistent and irregular narrowing shown by the small intestine study must be attributed to spasm. The physiologic mechanism by which the spasm was produced is not clear. It cannot be attributed to the unexplained generalized peritonitis because the effect of peritoneal irritation is to cause distention through over-stimulation of the sympathetics (Golden, 1950 for lit.).

In retrospect, the appearance of at least some of the narrowed loops is different from the usual appearance of regional enteritis. In the latter, the narrowing is relatively even and if the mucosal folds are exaggerated, the indentations they produce are usually not more than a few millimeters wide. It seems doubtful, however, that the same mistake in interpretation could be avoided in a similar case.

A study of these cases suggests that the earliest effect of amyloidosis of the intestine is a marked slowing of the transit time, and

that gas distention occurs late in the course of the disease.

The literature shows that amyloidosis may cause bleeding from the intestine. This may be slight as in Cases I and III, or may be severe.

CONCLUSION

The cases reported above show that either primary or secondary amyloidosis of the small intestine may cause: (1) thickening of the mucosal folds when the mucosa is infiltrated, (2) narrowing and irregularity of the lumen, roughly simulating the effect of chronic inflammation, such as regional enteritis, (3) gas distention when the tunica muscularis is sufficiently replaced, simulating ileus, either mechanical or paralytic, and (4) slowing of the transit time.

Gas distention seems to be the most common abnormality of the small intestine, in either primary or secondary amyloidosis. The literature thus far consulted has not mentioned the demonstration of roentgenological abnormalities simulating inflammation, shown in Case III.

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DISCUSSION OF PAPERS BY FRIEDMAN, MARSHAK, WOLF AND ADLERSBERG, AND GOLDEN

DR. LEON SCHIFF, Cincinnati, Ohio. I want to express my thanks for the privilege of reading and discussing these three interesting and stimulating papers. I have heard a rumor emanating from Minneapolis that Dr. Friedman is contemplating substituting a fluoroscopic couch for the fluoroscopic table.

I suppose if any of us discuss the World Series game being played today with any of our patients whose small intestine we are examining, we had better find out if we are talking to a Brooklyn or a Yankee fan.

While the literature contains scattered reference to the effect of emotions on small intestinal function, as Dr. Friedman has indicated, I believe his observations offer the most direct proof of such relationship in man, and should prove of steadily increasing importance.

The detailed studies of Dr. Marshak *et al.* should do much to renew interest in the subject of sprue and sprue-like syndromes, if only to see if the authors are right or not. It is important for the clinician to distinguish primary from secondary sprue syndromes for therapeutic and prognostic purposes.

I would like to discuss a case that we saw recently in a thirty-five year old Kentucky miner who had had typical sprue for five years, and a very severe form of the disorder.

We sent his films to Dr. Marshak, who felt that the changes were typical of primary sprue. Because of the presence of a pleural effusion and the possibility of a tuberculous etiology which would contraindicate steroid therapy, he was subjected to a laparotomy.

[Slide] This is an artist's drawing of the findings at laparotomy, which were very striking. There was enlargement of the mesenteric lymph nodes, many of which were 3 and 4 cm. in diameter and appeared yellowish. There was a marked distention of the mid-jejunum for a distance of about 7 cm. It was a sac-like dilatation, and the wall of the jejunum was a brownish-yellow and appeared emphysematous. On squeezing the emphysematous area small bubbles of gas could be seen to move freely under

the serosal coat and to dissect between the two leaves of mesentery. There were many other similar areas in the small intestine, but none as large as this one. The musculature of the small intestine was atonic, and the lumen filled with gas and fluid. In the lesser pelvis there was a small amount of free peritoneal fluid which was colorless and foamy and resembled soap suds.

A piece of the dilated area of jejunum measuring 2 cm. in length and 3 mm. in diameter was removed for biopsy, as were two mesenteric lymph glands. The lumen of the bowel contained frothy material not unlike that seen in the lesser pelvis. The mucosa was apparently intact in the region from which the biopsy was taken.

The biopsy specimen revealed a nonspecific inflammatory reaction in the mucosa, dilatation of the submucosal lymph sinuses, and deposition of considerable lipochrome pigment (probably lipofuscin) in the tunica muscularis. The lymph nodes revealed a chronic inflammatory reaction with dilatation of the sinusoids. Whipple's disease was excluded by special stains carried out by Dr. Black-Schaeffer of the Department of Pathology of the University of Cincinnati. Intestinal pneumatosis, which our patient presented, has been reported in conjunction with chronic enteritis, intestinal tuberculosis, and a variety of other conditions, according to a recent excellent review by Koss.

Having ruled out a tuberculous etiology, we proceeded with steroid therapy, which brought about temporary benefit.

I was particularly interested in the 3 patients of Dr. Marshak and his associates, who showed a normal small intestinal pattern. Was there anything distinctive about these three?

No mention was made of Whipple's disease in the discussion of differential diagnosis. Since this disease has recently been shown by Chester Jones and associates to respond, like sprue, to steroid therapy, its clinical differentiation from sprue may become more difficult. Have Dr. Marshak and his colleagues studied any cases of this disorder?

I would like to call attention to one pitfall in assessing the therapy of sprue, which I am sure the authors are aware of, namely, that many patients with tropical sprue improve on mere removal from the tropics.

Of much interest in the therapy of a disorder very closely related to sprue, namely, celiac disease, is a recent observation by British workers, including Frazer, of complete recovery of children with this disease on a wheat flour-free diet. Has Dr. Adlersberg tried this treatment in any of his adult cases of sprue?

The discrepancy between clinical improvement and persistence of the roentgen changes, so well emphasized by Drs. Marshak and Wolf, is of course challenging.

It is always a treat to listen to Dr. Golden talk about the small intestine. I was particularly interested in his clinical use of the response of the intestine to prostigmine and urecholine. You may be interested to know that our patient with sprue, with such heavy pigmentation in the muscularis, did respond to prostigmine given subcutaneously by lessening of distention and expulsion of gas, contrary to what I believe has been reported in other instances of sprue. We did not do roentgen kymographic studies at the time he was given the injections.

I would like to suggest one procedure that may be of considerable help in the diagnosis of secondary amyloidosis, namely, needle biopsy of the liver. The liver is much more frequently involved in the secondary cases than it is in the primary, where biopsy of the gum, as Dr. Golden mentioned, is more apt to show the presence of amyloid.

DR. FRED J. HODGES, Ann Arbor, Michigan. I suspect that Dr. Friedman has been guilty of violating those tenets of a physician-patient rapport which radiologists have learned to develop in order to facilitate gastrointestinal examination. He has done it purposefully, the better to demonstrate to what extent emotion is reflected in the alimentary behavior.

The striking intestinal reflections of emotional upheaval which he has shown can constitute a serious handicap to effective examination, and represent sound reason for the diligent attempts to sooth the patients being examined, whatever device may be employed.

It strikes me as being a reverse approach to the problem with which we are all so familiar. Years ago I learned from Dr. Harry Weber and his teachers the great importance of effacing one's own personality in the presence of the patient to be examined, and to employ whatever devices came to mind and seemed to be effective in the individual patient in order to reverse the situation that Dr. Friedman told us about.

The younger the radiologist, the more certainly he will fail in that attempt and will try

to be impressive by speaking with great formality in discussing medical matters. Unless he is careful he will unwittingly produce the responses that Dr. Friedman observed. It has been interesting to have our attention called once more to the very great effectiveness of emotion on the behavior of the intestinal tract.

Dr. Marshak has shown us, as on other occasions, gorgeous film demonstrations of small intestinal dysfunction and contrasting inflammatory anomalies. It is perhaps desirable at this point to call attention to the remarkable fact that in the vast majority of individuals a truly fabulous, highly complicated functional behavior is found to follow a characteristic pattern.

It is always a source of wonderment to me why and how the full length of the intestinal tract can behave in such similar fashion in widely differing individuals, and why it is relatively so seldom that the small intestine behaves as Dr. Marshak has shown in his highly selected cases.

Much has been done in radiology to explore the underlying reasons for disturbance of the characteristic behavior of the small intestine. Much remains to be learned. One wonders to what extent initially purely functional disorders are subsequently converted into nonreversible lesions.

Some of the work that Dr. Golden has done, has brought to light autopsy material showing definite organic neurological disease in nerve tissue and in the spinal cord associated with functional disturbances. We have had occasion to find a few such individuals from whom neurological specimens had been obtained, and there was no reason to believe that initially there had been purely functional derangement ultimately converted to irreversible pathologic states.

Dr. Marshak's case material goes a great distance toward clarification of the significance of reliable signs which represent purely functional as opposed to organic small intestinal anomalies.

Over recent years Dr. Golden has been responsible—with the best of intentions, I am sure—for creating a state of frustration on the part of the gastrointestinal radiologists. He has shown us how necessary it is to learn more about this extremely complex situation. His repeated teachings are slowly producing results and stimulating greater roentgenologic interest in this field.

All of us, I presume, can remember those days when we were purely organic diagnosticians, and anything that could not be shown graphically to be an organic lesion in the intestinal tract was beyond us. I certainly was one of those persons, and was very slow to become excited about the use of roentgen methods for the study of function. Those days have long since passed, and we are well aware of the fact that radiology can play an extremely important part part in discovering and studying purely functional disturbances.

Today Dr. Golden has presented yet another condition to be considered in the matter of small intestinal diagnosis.

DR. MARSHAK (closing). I would like to thank the discussers for their remarks. In answer to the first question, we have not seen the complication of pneumatosis intestinalis in our series of cases of ileitis and ileojejunitis. In answer to the second question, inflammatory changes in sprue are uncommon and our pathologists have not reported this finding. Striking anatomic changes which could be the basis for the disturbed intestinal function have not been observed. Interpretations of inflammatory changes may merely be evidence of a degenerative process.

Whipple's disease was not discussed as I have had very little experience with this particular entity. One case that was observed in our clinic revealed a normal small intestinal series. I have seen a case elsewhere with a pattern of immediate segmentation, slight dilatation and some increased secretions. The findings suggested one of the variants rather than typical changes we have described.

As yet, our experience as to the effect of the wheat-free treatment on celiac disease is insufficient.

The effect of steroid therapy clinically is dramatic. In only a few instances, however, was there an improvement in the pattern of the small intestine to the present time. This may be due to an inadequate length of follow-up study. It would seem likely, however, that the treatment is nonspecific.

DR. GOLDEN (closing). Dr. Friedman and Dr. Marshak have given us two most interesting

papers. I would like to mention just two or three points.

About five years ago Dr. Teitelbaum of New Orleans brought to the Presbyterian Hospital some of his films showing functional intussusception of the small intestine in children. Both John Caffey and I were convinced that we had been missing this interesting disorder of motor physiology. Since then we have picked up several such cases. It can occur in a number of different conditions, including emotional disorders. Dr. Caffey has picked up some examples in celiac disease. On Dr. Friedman's last slide, I thought a loop of intestine was shown which I would have interpreted as functional intussusception. This is a perfectly good physiologic explanation for the abdominal pain which occurs in these cases. The emotional disorders associated with diarrhea which I have seen occurred usually with marked hypermotility, the barium getting into the cecum in fifteen minutes, for example.

Dr. Marshak remarked that the saline suspension of the barium in itself produces an abnormal appearance in the mucous membrane. This has not happened in my experience. In personal discussion with him I find that he uses a relatively large amount of saline, whereas we use only 5 oz., in which 4 oz. of barium sulfate is suspended. I have seen no evidence that this amount produces the changes that he mentioned.

This topic is most stimulating and important. Both Dr. Friedman and Dr. Marshak are to be complimented on the work that they have shown us. I hope some day a panel discussion will be arranged which will give us about three hours in which to deal with this topic.

OBSTRUCTION OF THE SMALL INTESTINE IN INFANTS AND CHILDREN

A ROENTGENOLOGIC AND PATHOLOGIC STUDY*

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THIS study concerns acute obstruction of the small intestine occurring in infants and children up to fifteen years of age. Until recently, interest in obstruction of the small intestine in infants and children was limited to a study of the pathology. With advances in pediatric surgery and roentgenology, emphasis has shifted to early diagnosis and treatment. Careful and accurate analysis of the roentgenogram of the abdomen has proved a valuable method of early diagnosis in these cases.

REVIEW OF LITERATURE

Many investigators have emphasized the role of the abdominal roentgenogram in the diagnosis of intestinal obstruction. Schwarz, in 1911, first suggested its use in such cases. Spriggs, Assmann, and Marcuse also described the roentgenologic findings in intestinal obstructions. Case proved that accumulation of air alone provides adequate contrast in cases of intestinal obstruction and wrote extensively on the value of the plain abdominal roentgenogram. In 1927, Kalbfleisch emphasized the importance of abdominal roentgenograms made with the patient in the erect position.

Experimental studies provide the basis for recognition of the characteristic findings of intestinal stasis on the abdominal roentgenogram. Magnusson demonstrated that air normally passes through the entire gastrointestinal tract in as little as thirty minutes. Because of this rapid transit, obstruction of the intestine produces significant accumulation of air relatively early. This is of primary importance in the early diagnosis of small intestinal obstruction.

The first studies of artificial ileus, produced in dogs, were carried out by Wangensteen and Lynch. They demonstrated that accumulation of intestinal air was synonymous with intestinal stasis. In later studies, Wangensteen found accumulation of air in four to five hours following obstruction and proved that distention of the bowel was due to swallowed air. Ochsner concluded that accumulation of gas could be demonstrated as early as one hour after strangulated and three hours after simple obstruction.

Wasch and Marck studied the air content of the gastrointestinal tract of 50 normal newborn infants. They found that air normally enters the stomach with the first respiration. In 7 of 10 infants, air could be seen in the proximal portion of the small intestine within one hour. After three hours, almost all infants had air throughout the small intestine and colon. After four to eight hours, increasing

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† The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

amounts of air entered both the small and the large intestine. After eight hours, the amount of air in the colon decreased. This study strongly suggests that small intestinal obstruction may be diagnosed in many cases as early as three to four hours after birth.

Visible accumulation of air in the small intestine of infants and children up to three years of age is common. After this age, the air becomes mixed with the intestinal contents and is no longer normally visible.

INTERPRETATION

There are two findings on the abdominal roentgenogram which suggest early intestinal obstruction. These are sharp turns of gut containing trapped air, and evidence of increasing accumulation of air on serial films. In one study on infants and children, a "squaring off" of small intestinal loops accompanied by hairpin turns was found diagnostic of early obstruction.[41] The later findings of "layering" or stepladder patterns are well known in cases of obstruction. Ideally, the roentgenographic diagnosis should be made before these stages are manifest. Fluid levels can also be demonstrated in almost all these cases with the use of appropriate positions.

Because gastrointestinal air can normally pass in only one direction, observation of the amount and location of air in the colon must be noted on the abdominal roentgenogram. Recent investigations[23] have shown gas present in the colon in 50 per cent of the cases of small intestinal obstruction. In 20 per cent of the cases air was conspicuous, while in 30 per cent it could be seen only after careful study. Obstruction in the upper part of the small intestine is often associated with absence of air throughout the gastrointestinal tract.

Other conditions may present confusing findings on the abdominal roentgenogram. Small amounts of gas, with or without fluid levels, may be seen normally in the stomach, first portion of the duodenum and the terminal portion of the ileum. Patients with aerophagia may show scattered accumulations of air throughout the small intestine. Typical findings may be absent in intestinal obstruction when all accumulated air and fluid have been removed by suction. Collections of air may be seen in the jejunum in patients with gastroenterostomy. In some cases of large bowel obstruction, gaseous distention of the small intestine may be present.[2] Retained enemas often produce fluid levels in the distal part of the ileum. Fluid levels may also be seen in a variety of conditions, such as regional ileitis, gas-forming abscesses, mesenteric thrombosis and enterocolitis.[28]

PRESENT STUDY

As a basis for this study, the records of all cases of obstructive lesions of the small intestine encountered at the Mayo Clinic in the years 1942 through 1951 in the age group 0 to 15 years were reviewed. Only proved cases were accepted, and obstructions secondary to duodenal ulcer and those intussusceptions not limited to the small intestine were excluded. There remained 66 cases for study.

Clinical details and descriptions of the pathologic findings at the time of operation

TABLE I

OBSTRUCTION OF THE SMALL INTESTINE IN INFANTS AND CHILDREN: SUMMARY OF DATA

Etiologic Group	Cases	Deaths	Abdominal Roentgenograms	
			Examined	Diagnostic
Intrinsic causes	8	5	5	5
Extrinsic causes	23	9	14	14
Meconium ileus	3	1	2	2
Meckel's diverticulum	3	0	2	2
Adhesions	20	5	9	8
Cysts, tumors	3	1	2	2
Infections	5	2	3	3
Foreign bodies	1	1	0	—
Total	66	24	37	36

TABLE II

INCIDENCE OF INTESTINAL OBSTRUCTION ACCORDING TO AGE IN INFANTS AND CHILDREN

Age	Cases
Birth through 7 days	16
1 to 6 weeks	11
6 weeks to 1 year	5
1 to 3 years	7
3 to 5 years	8
5 to 15 years	19
Total	66

were recorded. Surgical and necropsy specimens were studied in 22 cases. All roentgenograms were reviewed in every case. The studies made with the aid of barium and the roentgenograms of the abdomen were separated for more careful analysis. Each roentgenogram was then reinterpreted without the benefit of a detailed history or knowledge of the pathologic findings.

The terms "air" and "gas" in regard to intestinal obstruction have been used interchangeably throughout this study. Air is probably the more appropriate term and is preferred.

Table 1 gives a general summary of the findings. Among the 66 cases there were 24 deaths, giving a mortality rate of 36.4 per cent. Almost two-thirds of all the obstructions were secondary to incomplete intestinal rotation or to adhesions. Abdominal roentgenograms, reviewed in 37 of the 66 cases, revealed intestinal obstruction in all but 1 of the 37 cases.

The incidence of intestinal obstruction, according to age, is given in Table II. In 27 cases the obstruction occurred in the first six weeks of life. There were approximately as many cases in infants in the first week of life as there were in children from one to five years of age.

In the ensuing pages we shall present our data on the basis of the etiologic categories of obstruction given in Table 1. With regard to each category we shall, as a rule, present (1) a general comment including certain points made by other authors and (2) the specific observations made in our own series of cases.

INTRINSIC OBSTRUCTION

The term "intrinsic" is used to include congenital obstruction due to atresia or stenosis. Although distinct differences do exist, this grouping is convenient and sufficiently accurate. Atresia implies a complete obstruction which terminates as a blind sac. Stenosis, when uncomplicated, produces only partial obstruction. Atresia is more common and occurs most frequently in the ileum and duodenum. More than half of the stenoses are found in the duodenum.

Developmental errors are usually considered the cause of these obstructions. In the embryo, the intestinal lumen is patent to the fifth week. Following this, there is a normal epithelial proliferation with obliteration of the lumen. By the twelfth week, vacuoles normally appear, coalesce, and again establish the permanent lumen. An error in or incompletion of this process produces an intrinsic obstruction which may be complete or partial.

The incidence of these obstructions is 1 in 20,000 births.[35] Cohen reported a slightly higher incidence. The most frequent sites are the lower part of the ileum and the duodenum. Obstruction is multiple in 15 to 25 per cent of cases.[12]

TABLE III

INTRINSIC OBSTRUCTION OF THE SMALL INTESTINE IN INFANTS AND CHILDREN: STENOSIS

Sex	Age	Site of Obstruction	Roentgen Findings
M	15 da.	Duodenum, third portion	Barium study: retention
M	1 mo.	Duodenum, second portion	Duodenal obstruction
M	1 da.	Duodenum	Duodenal obstruction
F	1 mo.	Duodenum, first and second portions	No roentgenograms

Table IV

INTRINSIC OBSTRUCTION OF THE SMALL INTESTINE IN INFANTS AND CHILDREN: ATRESIA

Sex	Age	Site of Obstruction	Roentgen Findings
F	Newborn	Duodenum, first portion	Obstructive lesion demonstrated elsewhere by barium study
M	4 da.	Ileum	Ileal obstruction
F	1 da.	Ileum with volvulus	Ileal obstruction
M	5 mo.	Ileum, distal portion	Ileal obstruction

Atresia almost always produces vomiting the first day of life. This is soon followed by dehydration and its consequences and, later, by distention in many of the cases. Stenosis, when severe, produces symptoms in the majority of cases in the first week. Patients with mild degrees of stenosis may be asymptomatic for months or years.

Farber's test of intestinal patency may be of value in these cases.[18,52] The result of this test is positive if a smear of the infant's meconium shows no exfoliated squamous cells. With careful technique, this finding is diagnostic of intestinal atresia. In the event squamous cells are wiped from the buttocks, a false negative result may be obtained.[32]

Present Series. An analysis of the cases of atresia and stenosis in our series is given in Tables III and IV. There was 1 patient with duodenal atresia, 3 with ileal atresia, and 4 with duodenal stenosis. One of the patients with atresia of the ileum had previously undergone an ileocolostomy elsewhere. The abdominal roentgenogram indicated small intestinal obstruction in the 5 cases in which it was used.

The close correlation between pathologic and roentgenographic findings in the second case of duodenal stenosis listed in Table III is shown in Figure 1.

EXTRINSIC OBSTRUCTION

Intestinal obstruction due to extrinsic causes is inseparably related to embryologic aspects of intestinal rotation. In the fifth week of development, there is rapid enlargement of the liver and abdominal contents. With this growth, the midgut, which includes the bowel from the duo-

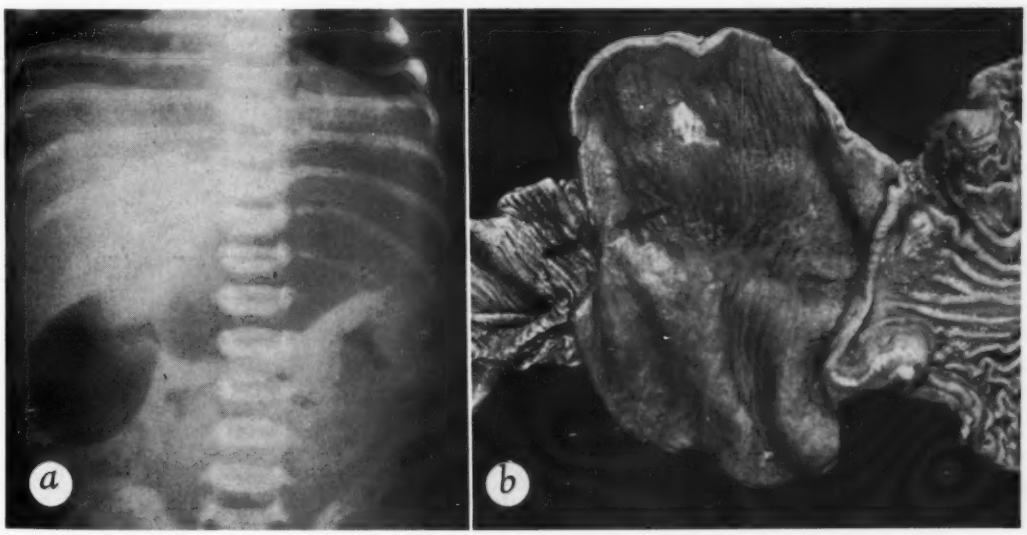

Fig. 1. Male infant with marked duodenal stenosis. (*a*) Preoperative abdominal roentgenogram showing the dilated stomach and first portion of the duodenum. (*b*) Pathologic specimen. A probe marks the site of stenosis.

denum to the midtransverse colon, is forced out into the base of the umbilical cord. By the tenth week, this segment undergoes a normal rotation in the process of returning to the abdominal cavity. The prearterial segment, which includes that portion of intestine proximal to the vitelline duct, returns first and passes right to left posterior to the superior mesenteric artery. The lower, or postarterial segment, rotates left to right and passes anterior to the superior mesenteric artery. Thus, a rotation through 270 degrees takes place in a counterclockwise direction. The duodenum is placed behind the superior mesenteric artery. The remaining portion of gut involved in the rotation lies anterior to the superior mesenteric artery.

At this time, the midgut is attached to the posterior peritoneum by a very narrow mesentery at the origin of the superior mesenteric artery. The midgut then normally fuses with the parietal peritoneum, giving the normal oblique attachment of the mesentery of the small intestine. The remaining portions of the colon also fuse and acquire their normal attachment to the parietal peritoneum.

Although "malrotation" and "incomplete rotation" are used interchangeably, the latter is preferred. It more accurately describes the process responsible for extrinsic obstruction. Anomalies of lesser severity include a narrow mesentery for the small intestine and a freely mobile cecum.

Because of incomplete rotation, the cecum may occasionally lie directly over the duodenum and produce obstruction by external pressure. More commonly, the congenital bands which normally support and fix the displaced cecum produce obstruction in the second and third portions of the duodenum. These bands are peritoneal reflections which impinge on the duodenum in their attachment to the right posterolateral abdominal wall.

If there is failure of development of the normal mesentery of the small bowel, volvulus may occur. This may be found alone or accompanying the duodenal obstruction described above. Volvulus produces mechanical obstruction of the bowel by compression. In some instances, serious interference with the blood supply may be present.

"Reversed rotation" has been described by Warthen, Lattman and White. They tabulated reports of 27 such cases and found that volvulus had occurred in 22 of the patients. In this anomaly, rotation takes place through 90 degrees in a clockwise direction. This places the duodenum anterior and the transverse colon posterior to the superior mesenteric artery.

The clinical manifestations of extrinsic lesions may be delayed. Although many remain asymptomatic for some time, Ladd and Gross found that the majority caused symptoms by the age of three weeks. Van Creveld has said that volvulus may produce recurring attacks of vomiting in older children. Wakefield and Mayo concluded that mesenteric bands producing obstruction in adults are always congenital in origin.

Present Series. The details of extrinsic obstruction in our series of cases can best be examined in Table v. There were 23

TABLE V

EXTRINSIC OBSTRUCTION OF THE SMALL INTESTINE IN INFANTS AND CHILDREN

Cause of Obstruction	Cases	
	Total	Abdominal roentgenogram diagnostic*
Duodenal bands	6	2
Volvulus	9	7
Duodenal bands and volvulus	3	2
Cecal pressure, obstruction of duodenum	1	1
Jejunal bands	2	1
Ileal band	1	1
Band extending from transverse colon to posterior peritoneum	1	0
Total	23	14

* Roentgenograms were diagnostic in all cases in which they were available for study.

cases of extrinsic obstruction occurring in 22 patients. Males and females were equally affected. The average age was greater than for the group of intrinsic obstruction. Twelve patients (54.5 per cent) were one month or less of age, and half of these were newborn infants. The ages of the remaining patients ranged up to ten years. More than a third of the patients had undergone previous surgical treatment.

Volvulus occurred 12 times in the 23 cases. Interference with the blood supply was noted in only 2 cases. In the case tabulated for the last item in Table v, a band extending from the transverse colon to the posterior peritoneum had trapped several loops of small intestine to produce obstruction.

A roentgenographic diagnosis of obstruction could be made in all 14 cases in which a preoperative roentgenogram of the abdomen was available for study. The roentgenogram in 1 of the cases of volvulus is shown in Figure 2.

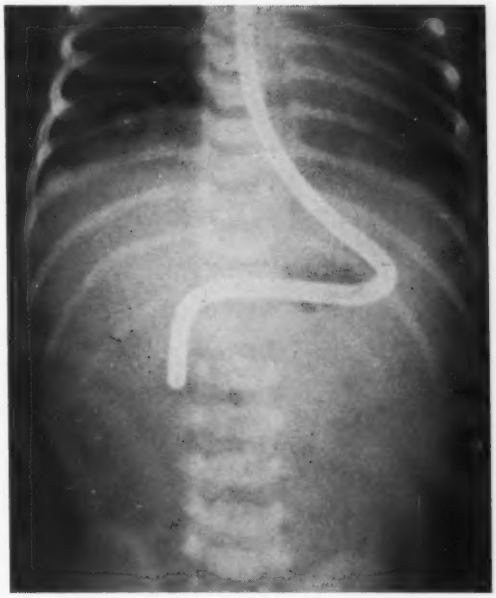

Fig. 2. Roentgenogram of the abdomen of a male infant with obstruction of the duodenum by a congenital band. The absence of air in both the small and the large intestine is striking.

MECONIUM ILEUS

Meconium ileus is complete or partial obstruction of the intestine in the newborn infant resulting from inability to propel physically altered meconium. Although recognized for many years, it has received little attention until recently.

Dodd in 1936 was able to find reports of only 16 cases in the literature. In a recent report, Bruwer and Hodgson cited 65 cases of meconium ileus associated with cystic fibrosis of the pancreas.

Landsteiner is credited with first associating this type of obstruction with pancreatic disease, in 1905. Andersen studied a large necropsy series of cases of cystic fibrosis of the pancreas and divided the patients into three clinical groups. One of these groups included those patients with meconium ileus.

Meconium ileus is almost invariably associated with pancreatic achylia, but there is evidence that other factors may play a role in the pathogenesis.

Dodd found in the literature reports of 2 cases in which the condition was associated with biliary obstruction. In both cases the pancreas was reported as normal. Farber,[20] however, studied 34 infants with biliary obstruction and found no instance of meconium ileus. The pancreas was normal in each case. Meconium ileus has also been described as a complication of volvulus or ileocecal stenosis.[20] This, however, is an entirely different condition, according to Farber. Obstruction results from inspissated meconium which is not as sticky or mucilaginous as that seen in true meconium ileus. Bruwer and Hodgson have stated that intestinal atresia may occasionally be secondary to meconium ileus, and stress the intimate attachment between meconium and intestinal mucosa. Neurogenic imbalance also has been recognized as a factor in meconium ileus.[8,19]

Farber[20] has expressed the belief that in some cases meconium ileus in newborn infants is the result of congenital obstruction of the pancreatic ducts. In others it is caused by a generalized disease involving

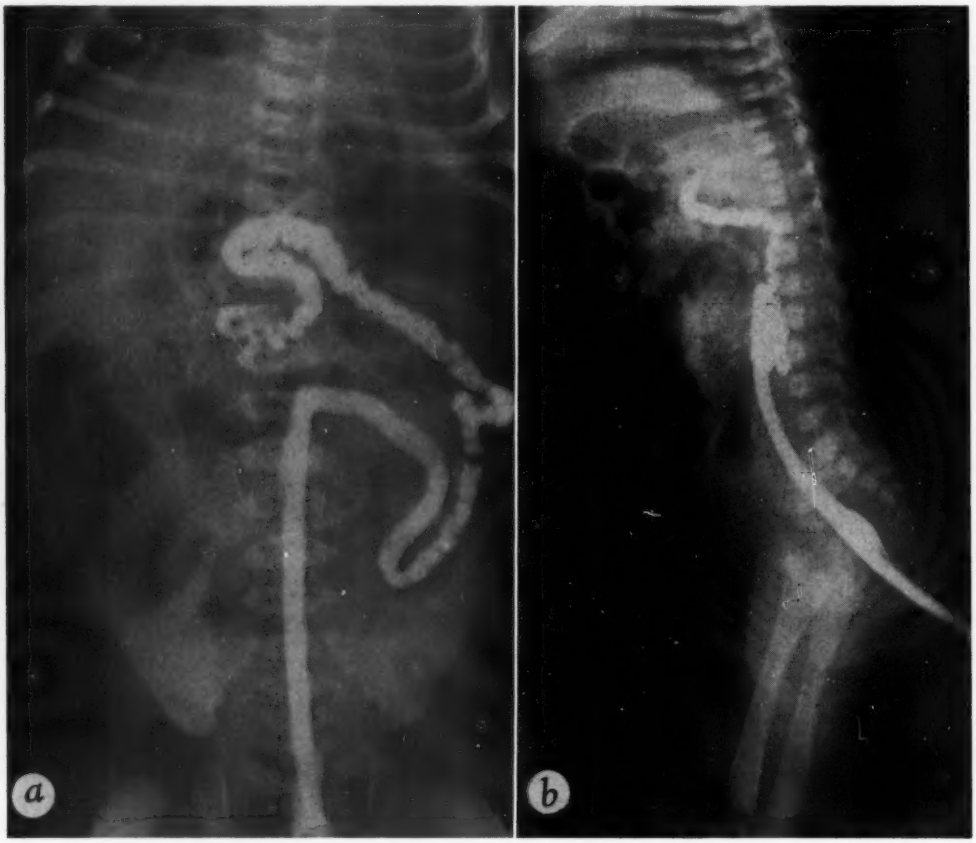

FIG. 3 (*a*) and (*b*). Anteroposterior and lateral views of a newborn female infant with meconium ileus. The entire small intestine is distended with air. A small, misplaced colon is disclosed by the barium enema.

chiefly the pancreas but, in addition, glandular structures in the upper respiratory, intestinal and biliary tracts.[19,21] In this systemic type of disease, a homogeneous, eosinophilic material within the pancreatic acini is responsible for obstruction of pancreatic secretion.

Wiglesworth explained the pancreatic achylia in meconium ileus as due to pancreatic atresia or failure of pancreatic development. Baggenstoss, Power and Grindlay recently studied 5 cases of fibrocystic disease of the pancreas. In every instance serial sections of the papilla of Vater and head of the pancreas revealed obstruction of the pancreatic ducts.

Clinically, meconium ileus resembles any other intestinal obstruction in the newborn infant. Cases have been reported in which recovery followed the passage of puttylike plugs.[15] Meconium peritonitis may be a complication in some cases. This may be suggested by discrete areas of calcification within the abdomen. The outlook is always poor. In some, the obstruction can be corrected, but the pancreatic lesion still presents a serious threat to prolonged life.

Present Series. There were 3 infants with meconium ileus in our series. In 2 cases, the point of obstruction was in the distal portion of the ileum. In the third case, obstruction occurred in the jejunum. Volvulus of the small intestine was present in the latter case. An ileocecal atresia was at least in part responsible for the inspissated meconium in 1 of the infants with ileal obstruction.

Roentgenograms of the abdomen were available for analysis in 2 of the cases.

Both revealed obstruction in the distal part of the small intestine. The abdominal roentgenograms in 1 of these cases are shown in Figure 3.

MECKEL'S DIVERTICULUM

Meckel's diverticulum, or some other remnant of the omphalomesenteric duct, is present in 2 to 4 per cent of the population.[16,30,36] There are three ways in which this anomaly may produce intestinal obstruction: (1) the diverticulum may be the leading point in intussusception, (2) it may, through an attachment to the umbilicus, produce a band which obstructs the intestine or (3) it may provide a point around which volvulus may occur.

Ulceration, inflammation and obstruction of the intestine are the most frequent complications of Meckel's diverticulum. In one study intestinal obstruction was reported as occurring in 9 of 14 cases of Meckel's diverticulum with complications. Intussusception was the most frequent cause of obstruction.[16]

Present Series. There were 3 cases of intestinal obstruction secondary to Meckel's diverticulum in our series of cases. In 2 instances, obstruction of the ileum was produced by compression from a band originating from this anomaly. In the remaining case, obstruction was due to intussusception of the diverticulum. Microscopic examination of the diverticulum in 2 of these cases disclosed no evidence of heterotopia. The ages of these patients varied from three weeks to seven and one-half years.

Abdominal roentgenograms were studied in 2 of the 3 cases and both revealed ileal obstruction.

ADHESIONS

Adhesions are a common cause of intestinal obstruction at any age. Wangensteen[47] has stated that they account for 30 to 40 per cent of all cases of intestinal obstruction. A great majority follow abdominal operations and, more specifically, appendectomy.

Fig. 4. Ileal obstruction secondary to adhesions. The small intestine is greatly distended and the pattern of "layering" is well shown.

The actual etiologic basis is not entirely clear, but most writers agree on two main sources: anomalies and infection. A third and equally important factor is the granulomatous reaction induced by magnesium silicate in the form of glove powder.[14] Golden has demonstrated changes within the intestinal wall underlying adhesions. This, he feels, produces a localized disturbance in the motor physiology which is manifested by narrowing of the lumen. This stenosis may contribute to obstruction in some cases. The usual methods of occlusion are by kinking, torsion or compression.

Present Series. Twenty patients in our series had intestinal obstruction secondary to adhesions. It is unusual that 18 of these patients were males. All but 1 of the 20 patients had undergone previous abdominal operations. The average age for this group was five years—greater than that for any other group in this study.

TABLE VI

OBSTRUCTION OF THE SMALL INTESTINE IN INFANTS AND CHILDREN: ADHESIONS

Site of Obstruction	Cases		
	Total	Previous operation	Preoperative abdominal roentgenogram
Small intestine, exact level not given	5	5	2
Jejunum	4	4	1
Ileum	11	10	6
Total	20	19	9*

* Roentgenogram diagnostic in 8 of the 9 cases.

The abdominal roentgenogram in 1 of these cases is shown in Figure 4. Acute angulation of the bowel and thickening of the mesentery are typical of obstruction attributable to adhesions.

Table VI provides additional information on the site of obstruction and the accuracy of abdominal roentgenograms in the diagnosis of such lesions. A diagnosis of intestinal obstruction could be made in all but 1 of the 9 cases in which preoperative roentgenograms were studied.

CYSTS AND TUMORS

"Mesenteric cyst" is a descriptive term which includes all cystic structures lying between the leaves of the mesentery or beneath the serosa of the intestine. Such cysts may occasionally produce intestinal obstruction.

Numerous attempts have been made to define and classify mesenteric cysts. Most often they are defined as cysts which are not malignant, parasitic or tuberculous and which do not arise from any normally placed retroperitoneal organ. One classification of mesenteric cysts which is both simple and useful is given by Ewing, as follows: (1) lymphatic (chylous) and serous cysts, (2) enteric cysts, (3) urogenital cysts and (4) dermoid and teratoid cysts.

The lymphatic, serous and enteric cysts are the most common. Even after gross and microscopic study they are not always easily distinguished. Both may show wide variations in size. The serous and lymphatic cysts are more often multilocular. Their wall is thin and usually consists of fibrous tissue with infiltration of lymphocytes. The wall may or may not contain dilated lymph spaces and bundles of smooth muscle.[5,7,27,38,42] Freeman has stated that serous cysts may contain smooth muscle bundles but that the chylous cysts have no muscular covering.

The origin of such cysts is not entirely clear. Ladd and Gross have said that they arise from misplaced bits of lymphatic tissue which proliferate and then accumulate fluid. Others[22,42] have expressed the belief that they are embryonic in origin or that lymph accumulates in a pre-existent cyst.

Enteric cysts most often originate from diverticula which have separated from the intestine or from localized, segmental duplications of the gut.[6,26] They may also arise from the vitello-intestinal tract or possibly from a misplaced Meckel's diverticulum.[22] They are intimately associated with the intestine and derive their blood supply from the same vessels.[6,7,42] They are more often unilocular and have a thicker wall than is present in the lymphatic or serous cysts. This wall frequently contains all the layers present in the intestine.[42]

Burnett, Rosemond and Bucher reviewed 200 cases of mesenteric cysts and found that one-fourth of all the cases occurred in infants and children less than ten years of age. Approximately half of all the cysts studied were located in the mesentery of the small intestine. Most of these were found in the mesentery of the ileum.

Mesenteric cysts most commonly produce symptoms by causing complete or partial intestinal obstruction.[6,24,42] Other complications which may be found include peritonitis secondary to rupture, hemorrhage into the cyst, torsion and incar-

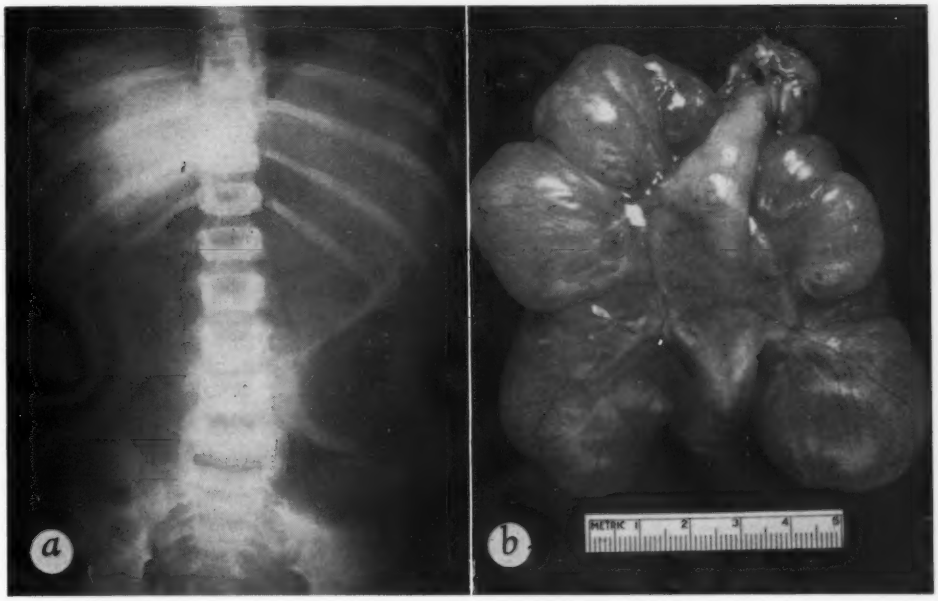

Fig. 5. Jejunal obstruction secondary to a mesenteric cyst. (*a*) The stomach is distended with air as are two loops of jejunum in the left midabdomen. There is a small amount of air in the colon. (*b*) Surgical specimen. The large mesenteric cyst is shown astride the jejunum. Obstruction resulted from compression.

ceration.[42] Occasionally a large cyst may produce symptoms because of pressure on other organs.

Roentgenologic studies may aid in the detection of these cysts. Caffey found that they may appear as shadows of water density displacing the intestine and stomach. Hinkel noted that they may produce areas of increased or decreased density on the plain abdominal roentgenogram. Careful gastrointestinal studies with opaque media may also aid in their diagnosis. In some cases, opaque inclusions may be present in the cyst, and in at least 2 cases calcification in their wall has been reported.[9,27]

Tumors of the small intestine of infants and children are rare. Benign growths which may be seen include leiomyoma, angioma, adenoma, lipoma and fibroma. Carcinoma in the small intestine of children is almost unknown; when found, it most frequently involves the duodenum. Lymphosarcoma is believed to be the most common malignant tumor of the small intestine in infants and children.[13] Lymphosarcoma more commonly affects males and is found most often in the ileum. Annular lesions are most common but polypoid growths may also occur. There may be multiple sites of origin in some cases.[43] The prognosis is always poor.

Present Series. There were 2 mesenteric cysts and 1 tumor of the small intestine responsible for obstruction in our series of cases. One of the mesenteric cysts was found in the jejunum. It was saddle-shaped and measured 10 by 5 by 4 cm. This produced sufficient pressure to obstruct the proximal portion of the jejunum. The roentgenogram of the abdomen and the surgical specimen in this case are shown in Figure 5.

The other mesenteric cyst involved the ileum. It had twisted upon itself to compress the intestinal wall secondarily. The cyst was biloculated and measured 8 cm. in its greatest diameter. Microscopic study of the cyst wall revealed bundles of smooth muscle with active fibrosis present.

In 1 case, a primary lymphosarcoma in the distal part of the ileum produced obstruction by ileoileal intussusception. Ap-

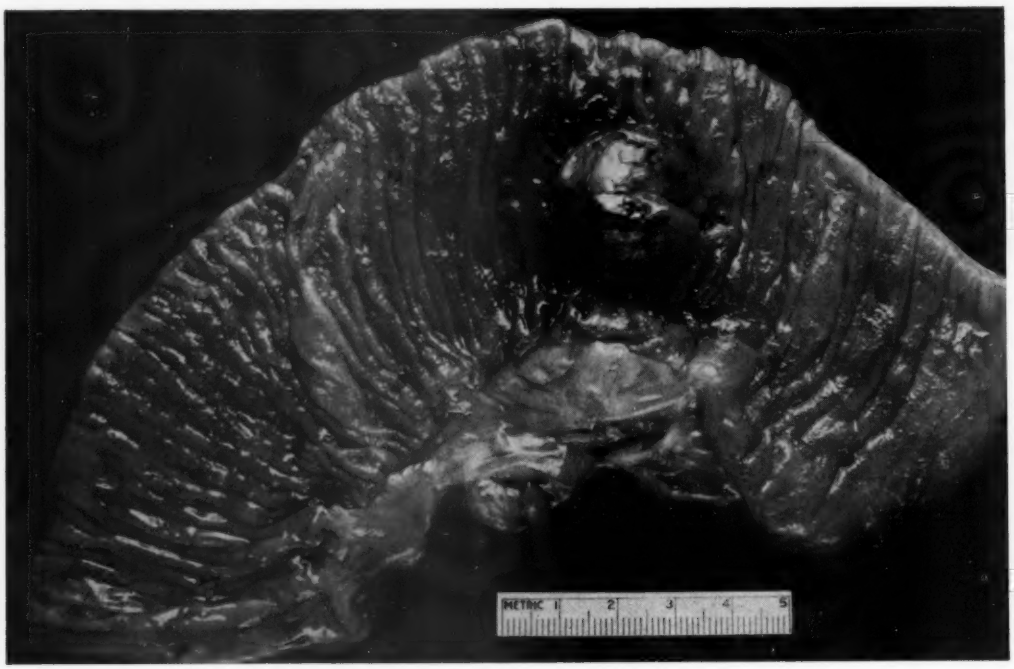

FIG. 6. Surgical specimen in a case of primary lymphosarcoma of the distal portion of the ileum.

proximately one-fourth of these tumors produce clinical symptoms in this way. This tumor was polypoid and measured 2.5 cm. in diameter. The surgical specimen is shown in Figure 6.

Roentgenograms of the abdomen were reviewed in both cases of mesenteric cyst. The findings were typical of obstruction of the small intestine.

INFECTIONS

Recent intra-abdominal infection was a primary factor in the intestinal obstruction in 5 cases in our series. In 3 of the cases, localized inflammatory masses produced the obstruction. The site was ileal in 2 of the cases and undetermined in the third. Adhesions were noted in only 1 of the cases. Abdominal roentgenograms were studied in 2 of these 3 cases and revealed intestinal obstruction in both instances.

In the remaining 2 cases, infection was generalized. Adynamic (paralytic) ileus was undoubtedly a factor in obstruction. The findings in 1 of the cases, however, suggested a mechanical type of obstruction.

FOREIGN BODIES

It is uncommon for foreign bodies to produce obstruction at any point in the gastrointestinal tract. In a large series, Ladd and Gross found that less than 5 per cent of the ingested foreign bodies even produced symptoms.

In 1 case in our series, a foreign body completely occluded the jejunum. This proved to be a ball of twine which measured almost 3 meters in length and produced a mass measuring 6 by 5 by 4 cm. Multiple small intestinal intussusceptions were noted proximal to the foreign body at the time of operation. Preoperative roentgenograms of the abdomen were not available for study in this case.

COMMENT

The diagnostic value of roentgenograms of the abdomen has been recognized for many years. The appreciation of air-fluid levels on roentgenograms made with the patient in the erect position and of air alone as contrast medium in intestinal obstruction is not new.

Additional studies have added to the value of the abdominal roentgenogram. Because air normally enters the gastrointestinal tract of infants shortly after birth, it is possible to detect congenital intestinal obstruction in newborn infants. Because air normally traverses the entire gastrointestinal tract rapidly, its accumulation always suggests intestinal stasis. If this pathway is blocked, the accumulation of air is clearly visible on the abdominal roentgenogram. This finding is present before clinical signs are clear. Laboratory studies have shown positive roentgenographic evidence of obstruction of the small intestine within one to three hours.

There are two findings on the roentgenogram of the abdomen which suggest early obstruction of the small intestine. The first consists of sharp turns of intestine dilated with air. The other reliable sign is increasing accumulation of air on serial roentgenograms. Air and fluid levels demonstrated on roentgenograms made with the patient in the erect position are also valuable evidence of obstruction. The later findings of stepladder ("layering") patterns and multiple air-fluid levels are characteristic of late intestinal obstruction.

The approximate level of obstruction can be determined in many cases. Variation in mucosal pattern, thickness of the bowel wall and general location of the affected segment are invaluable in reaching this decision. The ileal wall is thinner than that of the jejunum. Its mucosal folds are shallow and often obliterated by distention. The mucosal folds of the duodenum and jejunum are much deeper and are rarely, if every, obliterated by distention.

The presence of air in the colon formerly threw doubt on the diagnosis of mechanical obstruction of the bowel. From the findings in our study and from the experience of others,[23] this doubt is unwarranted. Small amounts of gas are commonly found in the colon in cases of mechanical obstruction of the small intestine and were present in more than 50 per cent of the patients in our series.

The differential diagnosis between obstruction of the small intestine and obstruction of the large intestine is based on several findings. The colon normally lies in the periphery of the peritoneal cavity. The mucosal lining is smooth and haustral indentations are visible. The small intestine is usually more central in location and its dilated coils more frequently lie in a transverse axis. Mucosal patterns of the small intestine are characteristic at upper and lower levels. In roentgenograms of the erect patient, fluid levels are often wider in the small intestine but of less vertical height than in the large intestine. Fluid levels in the small intestine are more likely to be central in location.

Mechanical and paralytic obstructions can be separated in most instances if clinical and roentgenologic findings are considered. Paralytic ileus is a common postoperative complication. In other instances it may follow trauma or intra-abdominal infections. In paralytic ileus, the degree of distention of the small intestine is usually not as great as in mechanical obstruction. Serial roentgenograms in cases of paralytic ileus show few changes taking place. In mechanical obstruction, serial roentgenograms show changes in the air-fluid levels and often show changes in the degree of small intestinal distention. The amount of gas present in the colon is usually greater in paralytic obstruction. In addition, if roentgenoscopic examinations are used, it is generally observed that movement of the diaphragm is limited or absent in cases of paralytic ileus.

Numerous conditions other than intestinal stasis may produce air-fluid levels on the abdominal roentgenogram. For this reason, a positive diagnosis of intestinal obstruction must always be supported by positive clinical findings. When the diagnosis is in doubt, serial roentgenograms will frequently settle the issue.

Abdominal roentgenograms of the patient in the supine and erect positions should be made routinely in every case in which obstruction of the small intestine is

suspected. In many cases posteroanterior and lateral roentgenograms of the erect patient will prove helpful. Such roentgenologic examination should always be made as early as possible. If the first examination gives inconclusive results, the procedure should be repeated every four to eight hours. Serial roentgenograms should be made as long as clinical signs persist, or until a diagnosis of intestinal obstruction has been made.

This examination does not often elicit the cause of obstruction of the small intestine. Some knowledge of the pathology of such obstructions in infants and children, however, will often aid in suggesting the most probable cause of the obstruction. In our series of 66 infants and children, the roentgenogram of the abdomen proved an accurate and simple means of early diagnosis. More general use of this diagnostic aid should be encouraged.

CONCLUSIONS

1. Air normally traverses the small intestine rapidly.

2. Obstruction of the small intestine may be diagnosed as early as three to four hours after birth.

3. Accumulation of air and fluid in the small intestine may be seen in many conditions other than intestinal obstruction.

4. The earliest roentgenologic signs of small intestinal obstruction are (a) sharp turns of intestine that contain air and (b) evidence of increasing amounts of intestinal air.

5. Significant accumulation of air and fluid occurs proximal to the site of intestinal obstruction within one to three hours.

6. Intestinal obstruction secondary to incomplete intestinal rotation and to adhesions has accounted for almost two-thirds of the cases.

7. The abdominal roentgenogram has proved a useful and accurate means of early diagnosis of small intestinal obstruction in infants and children.

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BENIGN GASTRIC ULCER OF THE GREATER CURVATURE

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BENIGN ulcers on the greater curvature of the stomach are supposedly a rather rare medical phenomenon. It has been axiomatic in medical teaching to regard all greater curvature ulcers as malignant and surgical.

In the September, 1950, issue of *Radiology* Friedman and Epstein[3] state that there had been only 24 histologically proved cases of benign ulcer of the greater curvature up to that time. They report 2 cases of their own, thus making a total of 26 proved cases.

This is a surprisingly small figure—only 26 proved cases of benign ulcer of the greater curvature up to 1950—and bears out the rarity of this lesion. It is undoubtedly true that there are many other cases which have not been reported.

It has been our good fortune to see and accumulate 6 cases of benign gastric ulcer of the greater curvature in the past few years. Two of these cases were seen at the University of Oklahoma Hospital.

Five of the cases have had surgical resection and are histologically proved to be benign. The other case has never come to surgery, so that it has not been microscopically proved. However, this patient was treated medically and has been followed for twelve months and the lesion has remained healed. Some authors (Buckstein[1] and Campbell[2]) report cases cured by medical therapy alone.

Review of our cases shows that there are no clinical criteria to differentiate benign ulcer from carcinoma. Age, history, duration and character of symptoms, free acid, and size of the crater were not of conclusive diagnostic significance. One of our patients was a female. The incidence of 1 female to 5 males closely agrees with the ratio found in all gastric ulcers regardless of location. The patients' ages range from thirty to sixty-four years. The duration of symptoms was from a few weeks to several months. The craters varied in size from a few millimeters to 3.5 centimeters.

From the roentgenologic standpoint the majority of the cases were reported as carcinoma or probable carcinoma. The presence of an ulcer on the greater curve of

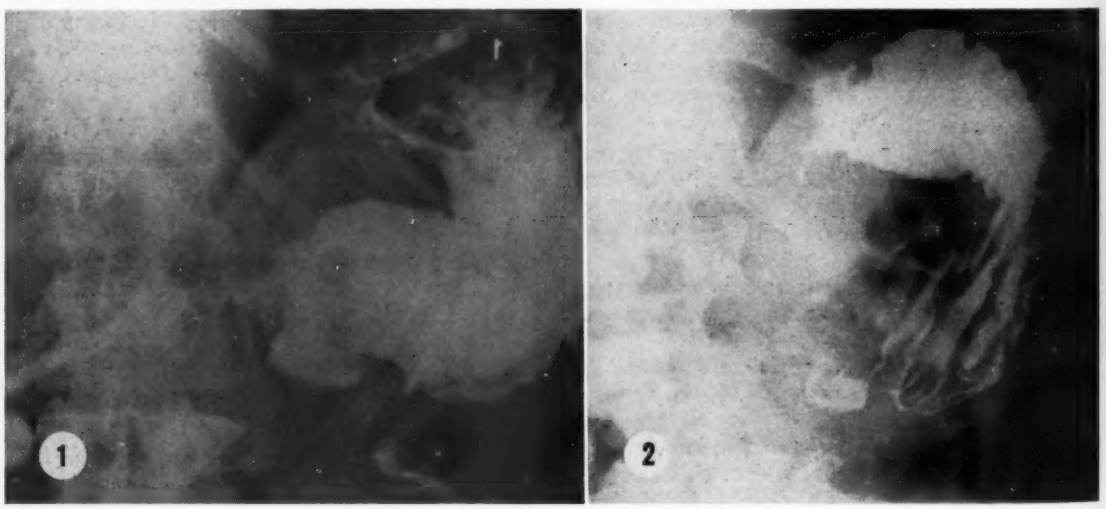

FIG. 1 and 2. Case 1. Large ulcer crater measuring 3 by 1.5 cm. on greater curvature of stomach. There was considerable spasm in the antral area and no peristalsis.

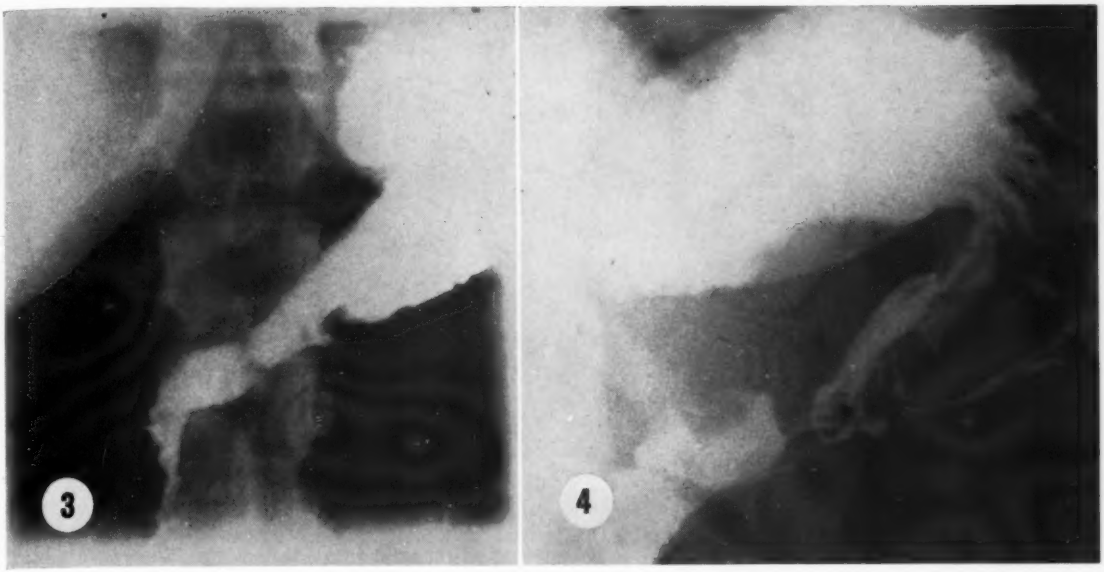

Fig. 3 and 4. Case II. Female, aged thirty, with ulcer on greater curvature at examination in March, 1950. Treated medically and apparently healed.

the stomach was often the main reason for suspecting malignancy, since several of these ulcers had benign characteristics. The main characteristic which suggested that the ulcer might be benign was the radiation of gastric folds into the crater with lack of infiltration and rigidity of the ulcer margins. Case IV (Fig. 11 and 12) is a good example of this finding, as is Case VI (Fig. 15 and 16).

REPORT OF CASES

Case I. E.R. This fifty-five year old white male was admitted to the University of Okla-

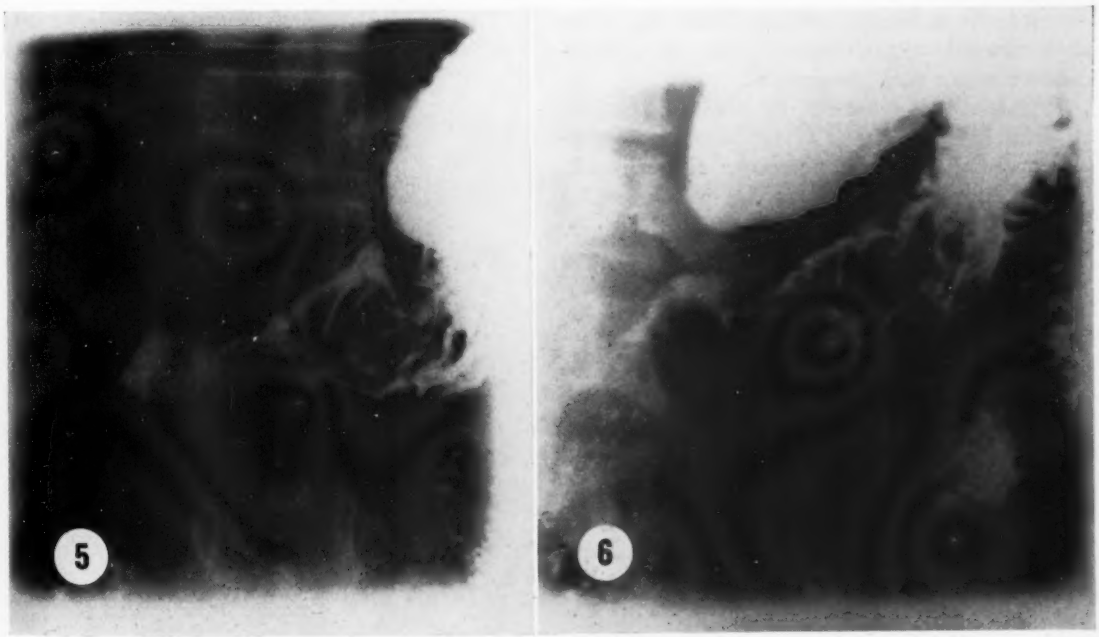

Fig. 5 and 6. Case II. Recurrence of the ulcer in January, 1951. At operation this was proved to be benign ulcer.

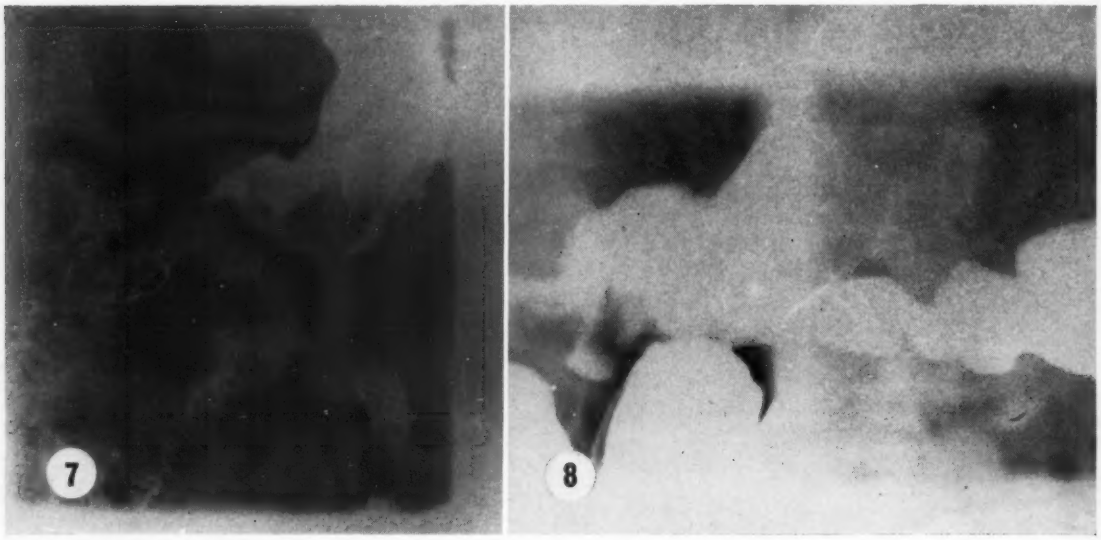

FIG. 7 and 8. Case III. Ulcer on greater curvature of stomach in forty-eight year old alcoholic. Notice rugal folds leading into crater in Figure 7.

homa Hospital on April 7, 1951, with the chief complaint of anorexia for six months, epigastric pain for one year, and loss of 25 lb. in weight in the past year.

Past history revealed "ulcer-like" symptoms dating back to 1939. No previous roentgen studies had been done. In 1947 the patient had had a cholecystectomy.

Physical examination was essentially normal except for tenderness and an indefinite mass approximately 2–3 cm. in the epigastrium which did not move with respiration.

Roentgen examination on March 22, 1951, revealed a large ulcer crater on the greater curvature of the antral portion of the stomach, approximately 4 cm. from the pylorus. The crater measured approximately 3 by 1.5 cm. and was quite tender to palpation. The antral portion of the stomach showed considerable spasm and no peristalsis was noted in this area. The rugal folds radiated into the crater and the walls seemed fairly pliable (Fig. 1 and 2).

At surgery on April 13, 1951, a firm mass measuring 2.5 cm. in diameter was found on the greater curvature of the stomach and this mass was densely adherent to the transverse colon. Large firm lymph nodes were present along the lesser curvature of the stomach extending to the cardia. A partial resection of the stomach and involved transverse colon was done.

The pathological diagnosis was chronic gastric ulcer and the lymph nodes revealed chronic lymphadenitis. There was no evidence of malignancy in either the resected stomach or lymph nodes.

CASE II. Mrs. R.F.D. This thirty year old white female was first roentgenographed on March 18, 1950, and an ulcer crater was found on the greater curvature side of the pyloric portion of the stomach (Fig. 3 and 4).

The patient was placed on medical treatment and was followed by roentgen examinations at

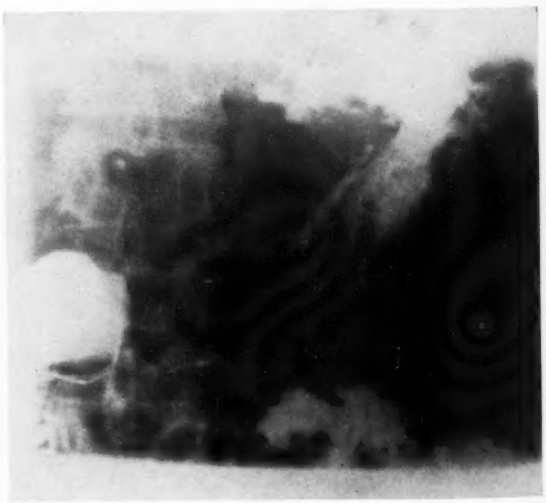

FIG. 9. Case III. Roentgenogram six weeks after medical treatment shows complete disappearance of the ulcer crater.

frequent intervals. Her symptoms of upper gastric distress and melena rapidly subsided and the ulcer was soon shown to be healed by the repeated roentgen examinations.

On January 13, 1951, the patient returned with a recurrence of symptoms and with the statement that the diet and medicine had not been taken for many weeks. Roentgen study at this time showed a recurrence of the gastric ulcer in the same location on the greater curvature (Fig. 5 and 6).

She was operated on January 23, 1951, and a subtotal gastric resection was done. Pathologically this ulcer was proved to be benign.

The patient has remained well with no recurrence of symptoms and was last seen on May 17, 1952.

Case III. H.L. This forty-eight year old white male was first admitted to Mercy Hospital on September 24, 1951. He stated that on the previous night he had vomited a great deal of red and "coffee-ground" blood. The vomiting continued until admission. A severe, constant, epigastric pain developed which radiated through to the back. For the past two months the patient has been taking a package of tums daily.

The patient is a chronic and severe alcoholic. Four years ago he was operated on at another local hospital and a pancreatitis was found. Two years ago he was examined at The Scott-White Clinic in Temple, Texas, and found to have cirrhosis of the liver, pancreatitis, potential diabetes and hypertension.

On physical examination the blood pressure was 120/70. The examination was negative except that the liver was enlarged, extending four fingers below the costal margin and there was extreme tenderness in the mid epigastrium. The admission blood count revealed a hemoglobin of 6.5 gm. and a red blood cell count of 1,900,000. The blood counts rose rapidly after transfusions and in one week were back to normal.

Roentgen examination on September 10, 1951, showed a large ulcer on the greater curvature of the stomach in the pyloric area (Fig. 7 and 8). This measured 16 by 10 mm. The patient was roentgenographed every two weeks and by October 19, 1951, no evidence of the ulcer could be found (Fig. 9). His last roentgen examination was on June 25, 1952. This examination was also negative with no ulcer (Fig. 10).

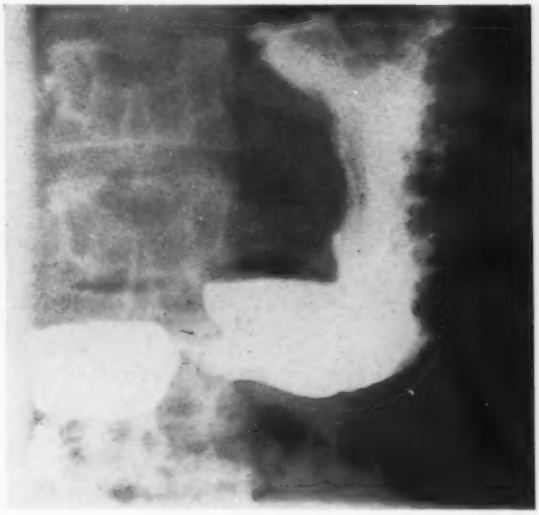

Fig. 10. Case III. Nine months after original examination, the gastric ulcer remains healed.

It was felt that this was a benign gastric ulcer and was treated medically. Since the original admission there have been several later admissions and discharges from the hospital. The patient has cooperated poorly and has continued to drink. Despite the lack of proper management the ulcer has remained healed with no recurrence for a period of one year.

This case has had no microscopic confirmation but has remained healed for one year which makes us feel that it is presumably benign.

Case IV. E.E.G. This thirty-three year old white male was admitted to Mercy Hospital on February 22, 1952. His chief complaints were epigastric pain, hematemesis, melena and a weight loss of 25 pounds in one month.

His previous history showed a hypertension of ten years' duration for which a bilateral Smithwick operation had been done three years previously. The patient had also had a bladder neck resection and an orchiectomy for abscess.

Roentgen examination revealed a large ulcer crater on the greater curvature of the mid-portion of the stomach which measured about 2 by 3 cm. Mucosal folds led into the crater and no infiltration was seen (Fig. 11 and 12).

The patient was operated on March 6, 1952, and the large ulcer crater was found and a subtotal gastric resection done. The ulcer was proved benign by microscopy.

The patient had a very stormy postopera-

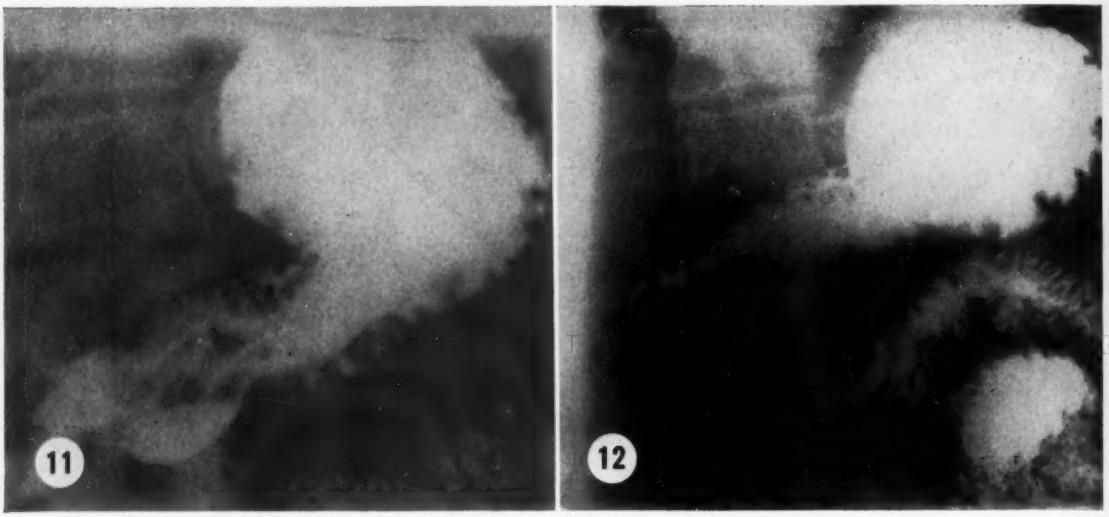

FIG. 11 and 12. Case IV. Large gastric ulcer measuring 2 by 3 cm. Note how the mucosal folds radiate into this benign ulcer.

tive course, with a myocardial infarct, severe bronchial pneumonia, acute parotitis, a massive gastric hemorrhage presumably due to surgery and dicumarol and finally by an incisional hernia. The patient recovered from all of these complications and was discharged on April 3, 1952.

CASE V. G.F. This patient is a white male who is now thirty-two years of age. He was first seen by his referring doctor in 1948, at which time he complained of a chronic stomachache of many years' duration. This was relieved to some extent by food and milk, but had constantly recurred.

Roentgen examination at this time revealed an active duodenal ulcer. He was placed on medical treatment and responded very well.

He was next seen in November, 1951, complaining of epigastric pain of one week's duration. His diet had been followed only occasionally during periods of pain. Roentgen examination again revealed an active duodenal ulcer.

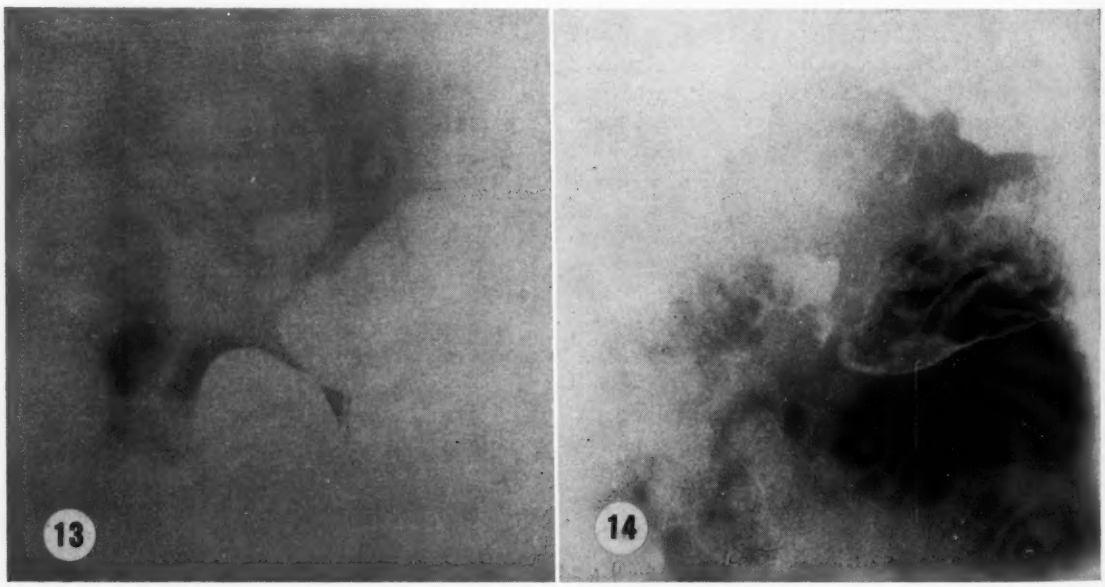

FIG. 13 and 14. Case V. Small prepyloric gastric ulcer on the greater curvature of the stomach. This failed to heal under medical treatment and a gastric resection was done. Microscopically this was benign.

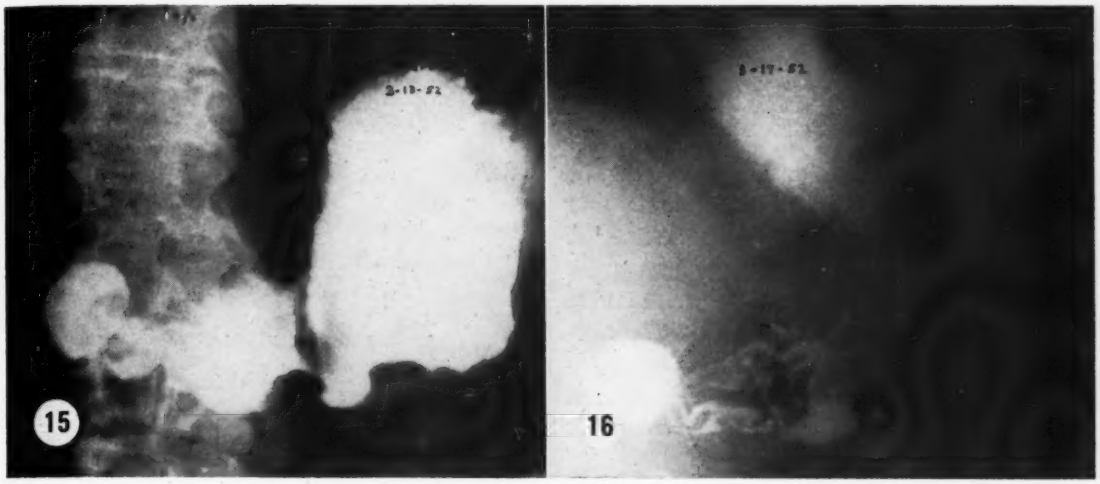

Fig. 15 and 16. Case VI. Large gastric ulcer on the greater curvature with marked induration and an apparent filling defect. Interpreted as malignancy.

On February 21, 1952, he stated that the pain was almost constant, being relieved for only one hour by milk and cream. He was awake every hour during the night.

Roentgen studies now revealed a small active ulcer crater on the greater curvature side of the stomach in the immediate prepyloric area (Fig. 13 and 14). There was no infiltration and little edema. The duodenal bulb showed its old deformity.

The patient was placed on bed rest and more active medical management. Periodic recheck roentgenograms showed no change in the appearance of the gastric ulcer.

He was operated on April 4, 1952, with a subtotal gastric resection. The specimen showed that the prepyloric greater curvature ulcer was not healed. The pylorus was scarred and the lumen was moderately constricted. Microscopic studies showed no malignancy in the ulcer.

Case VI. H.H. This sixty-four year old white male was admitted to the University of Oklahoma Hospital on March 14, 1952 with the history of vague upper abdominal pain for one year. Three weeks prior to admission this pain was noted more before meals and somewhat relieved by eating. He had had no indigestion, melena, and no weight loss. Milk diet failed to relieve his symptoms.

Physical examination by Dr. L. K. Chont, Ponca City, Oklahoma, disclosed a large ulcer crater of the greater curvature of the stomach with a constant filling defect at either side of the ulcer interpreted as malignancy with meniscus (Fig. 15 and 16).

Re-examination at University Hospital on March 17, 1952, again revealed a large ulcer of the greater curvature of the stomach.

At surgery on March 19, 1952, dense, generalized abdominal adhesions were encountered. A 4 cm. mass on the greater curvature of the stomach about 9 cm. from the pylorus was found and enlarged lymph nodes were present along the lesser curvature of the stomach. This was thought to be malignant and a complete gastric resection was done.

Pathological examination revealed no malignancy in the gastric ulcer or lymph nodes.*

SUMMARY AND CONCLUSION

Six cases of benign ulcer of the greater curvature of the stomach have been presented.

Although the majority of gastric ulcers of the greater curvature are malignant, roentgen examination does offer evidence that certain of these ulcers are benign.

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* Since this paper was accepted for publication the 6 patients have all been closely followed and are still living and well.

MUCOCELE OF THE APPENDIX*

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CYSTIC dilatation or mucocele of the appendix is not a rare disease. Over 500 cases are reported in the literature.[4] A preoperative diagnosis is, however, rarely made. In a search of available literature only 4 such instances were found. The purpose of this brief report is to present another case where a preoperative diagnosis was made, largely on the roentgenographic findings.

CASE REPORT

A thirty-four year old white woman was seen with complaints of low back pain and menstrual irregularity of five to seven years' duration. The patient had been married seventeen years and had never been pregnant. There were no colonic symptoms. Physical examination showed a small uterus. Neither ovary could be felt. There was a palpable, slightly movable and moderately tender mass in the right lower abdominal quadrant which was about the size of a lemon. Roentgenograms of the lumbosacral spine were negative. There was a partially calcified, comma-shaped mass in the right iliac fossa measuring approximately 3 by 3 by 8 cm. (Fig. 1). The calcium deposits were in the outer walls of this mass. The cecum and lower ascending colon were displaced medially. A constant, concave filling defect in the inferior and lateral portions of the cecum was demonstrated by a barium enema examination (Fig. 2). The upper medial end of the calcified shadow fitted into this cecal defect. This mass moved with the cecum and could not be separated from it. Neither the appendix nor terminal ileum could be filled with barium. The preoperative impression was a partially calcified mucocele of the appendix.

FIG. 1. Roentgenogram of right lower abdominal quadrant showing a tubular mass with irregularly calcified outer margins.

On July 15, 1952, the appendix was removed. It measured 4.5 by 5 by 10 cm. On sectioning the walls, a sensation of cutting through an eggshell was felt. The wall was 3 to 4 mm. thick and partially calcified. The lumen contained thick, viscid, amber colored, translucent, jelly-like material. On microscopic examination the epithelial lining of the appendix could be identified in only one small area. Its almost complete absence was thought to be due to compression atrophy. No inflammatory reaction was seen.

DISCUSSION

There are certain features of a mucocele of the appendix which should help in its diagnosis. Euphrat[5] in 1947 pointed these out: (1) if the cyst is large enough, it will produce significant displacement and deformity of the cecum; (2) if the cecum is mobile, the mass will move with it; (3) calcific deposits in the wall of the cyst are not infrequent; (4) the appendix does not fill with a contrast enema. In 1936, Åkerlund[1] had reported 2 cases which showed calcifications just inside the outer contour of the

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FIG. 2. This is a spot film made during barium enema examination. The cecum is displaced medially. There is a concave defect in the inferolateral portion of the cecum, and the upper portion of the calcified mass fits into this concavity. The two could not be separated by palpation.

tumor which resembled the picture found in "porcelain gallbladder" or "cholecystitis calcificans." He had failed to make a correct diagnosis, but felt that these characteristic roentgenologic findings should have led to such.

FIG. 3. A roentgenogram of the specimen.

FIG. 4. Photograph of the specimen.

Vorhaus[21] in 1930 described the first case in which the preoperative diagnosis of mucocele of the appendix was made correctly. In this patient barium entered the mucocele, probably through a re-established lumen. This return of patency must be an unusual occurrence since only one other case has been found in the literature.[10] In 1939, Varela-Fuentes *et al.*[20] reported

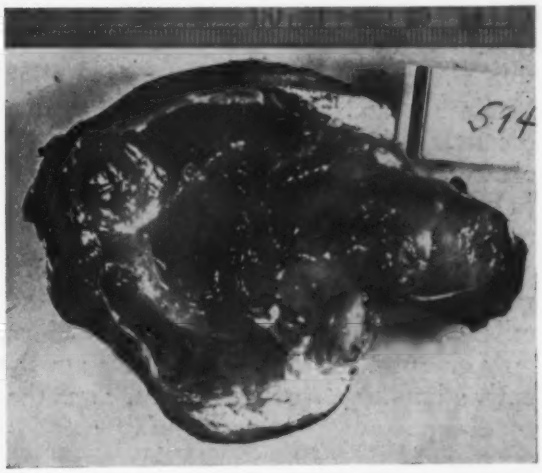

FIG. 5. Photograph of opened specimen. The mucoid material in the lumen was thick, sticky and did not flow from the lumen.

from Montevideo a case diagnosed preoperatively using Åkerlund's[1] criteria. Euphrat[5] in 1947 described a forty-two year old patient with an appendiceal mucocele measuring 8 cm. in diameter which was correctly diagnosed by this radiologist. This patient also had a pseudomucinous cyst of the right ovary which measured 5 cm. in diameter, apparently separate from and coincidental to the appendiceal lesion. Each tumor was resected. Bonann and Davis[4] in 1948 reported the fourth case diagnosed preoperatively. This tumor measured 8 by 11 by 11 cm. The case history recorded here is thought to be the fifth in this series of mucoceles diagnosed prior to operation.

An unusual triad of conditions are thought to be necessary for the formation of a mucocele of the appendix: (1) the cecal end of the lumen slowly becomes stenotic; (2) there is a continuous production of mucus; (3) there is an absence of significant infection. This narrowing of the lumen must be gradual. A rapid closure usually leads to acute appendicitis. Grodinsky and Rubnitz[6] experimentally produced appendiceal mucoceles in rabbits by ligating the appendix near its base after first cleansing its lumen, care being taken to preserve the blood supply.

The main complications of mucoceles of the appendix are: (1) rupture with production of pseudomyxoma peritonei; (2) torsion with gangrene and hemorrhage; (3) herniation and intussusception into the cecum causing varying degrees of bowel obstruction; (4) pressure on the right ureter to produce a hydroureter and hydronephrosis.

When there is rupture of a mucocele into the peritoneal cavity, some of its lining cells may be implanted. These seedings may give rise to cysts, which cysts apparently stimulate a reactive fibrosis. Then the condition known as peritoneal pseudomyxoma is thought to arise. Weaver[22] reported an incidence of 0.11 per cent in a series of 256 cases of appendiceal mucoceles. Rosenfeld[17] stated that of over 500 cases of peritoneal pseudomyxoma reported, more than four-fifths are thought to be of ovarian origin. Yet he felt that even when it seems almost certain that the condition is a pseudomucinous cystadenoma or cystadenocarcinoma of the ovary with peritoneal implants, one should consider a peritoneal pseudomyxoma of appendiceal origin and remove the appendix as well as the ovarian tumor.

SUMMARY

1. A patient having a mucocele of the appendix is presented. This is thought to be the fifth reported case where the preoperative diagnosis was correctly made.

2. The criteria necessary for such a diagnosis have been discussed. Knowledge of these criteria should lead more observers to consider the likelihood of such a lesion.

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ORAL CHOLANGIOGRAPHY WITH TELEPAQUE*

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RECENT investigation of telepaque as a cholecystographic medium has established its superiority over all other such media. This is evidenced by a minimal incidence of side reactions experienced by the patient, superior visualization of the gallbladder, good density and contrast, and rapid emptying of the gallbladder. The gallbladder has been visualized with telepaque when it failed to do so with other media.[4,6,8,15,18,19,23,24,25,26]

Even more gratifying has been the visualization of the bile ducts which occurred in about two-thirds of the cases in which the gallbladder was visualized.

The term "cholangiography," as used until recently, indicates a procedure conducted in conjunction with surgery of the biliary tract for the purpose of roentgen visualization of this tract. This procedure is more correctly spoken of as surgical cholangiography, and may be immediate, direct or operative, when performed in the operating room, during the operation, delayed or indirect when performed at any time after the patient leaves the operating room.

For visualization of the biliary tract without surgical intervention, but following the administration of telepaque by mouth, I have chosen the term "oral cholangiography."

It has long been our ambition to visualize the biliary tract in its entirety in a manner more or less comparable with the visualization of the urinary tract or digestive tract. We have come closer to this objective now than ever before.

Studying the effects of various medications on the sphincter of Oddi, many workers have attempted to produce relaxation by means of nitroglycerine, amyl nitrite and atropine, or have induced a spasm following injection of morphine or prostigmine.[2,9,16,21,22,28] As a result of the sphincteric spasm, bile carrying the radiopaque substance, which is used as a cholecystographic medium, is retained in the bile ducts for varying lengths of time for the duration of the spasm. This procedure did not prove to be as valuable as was anticipated, since artificial conditions have been induced which mask or make evaluation of a pre-existing spasm or obstruction difficult and unsatisfactory, and often causes discomfort and unpleasant reactions to the patient. The procedure was further limited by the low density of the contrast media which had been in use.

Visualization and investigation of the bile ducts, at first an incidental part of a cholecystographic examination, now constitutes a basic phase of the procedure as conducted in our department. It is felt at this time, however, that we have only touched the surface and barely explored the possibilities of what is developing into a significant procedure, and a definite milestone, in the investigation of diseases involving a triad consisting of the duodenum, the biliary tract and the pancreas. Further additions, developments and improvements in technique are certain to follow.

TECHNIQUE

The examination is performed as a part of, or in conjunction with, routine cholecystography. The preparation of the patient and the routine are essentially the same except for a few additional steps. A plain film is made the day before the examination. The same evening the patient takes 3 grams (6 tablets) of telepaque by mouth at about 9 or 10 o'clock. In the case of hospitalized patients, these may be taken after supper in order to suit the convenience of the nurses and hospital routine.

* Presented at the Seventh International Congress of Radiology, Copenhagen, Denmark, July 19–25, 1953.

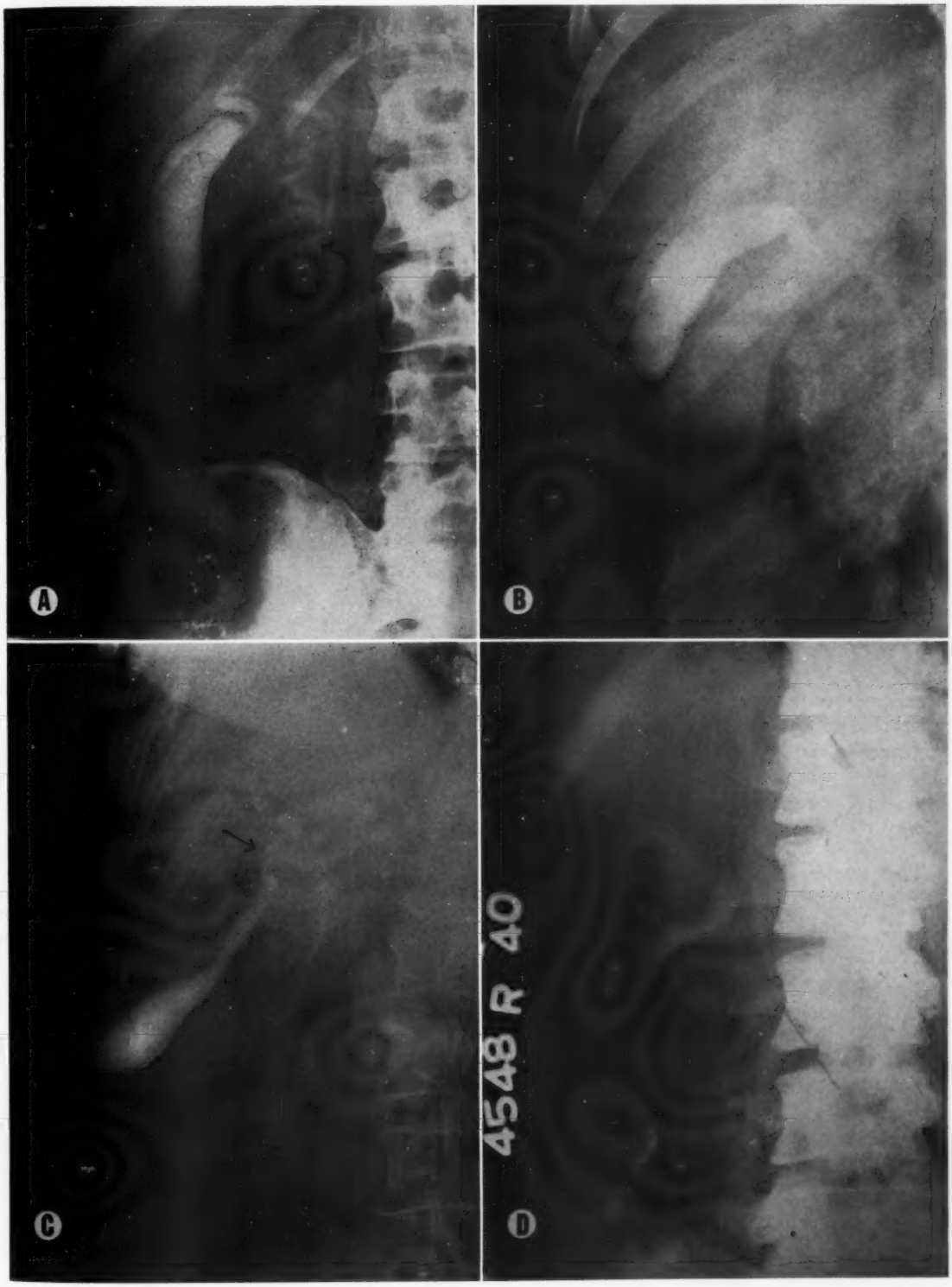


Fig. 1. (*A*) (*B*) (*C*) (*D*) Various normal ducts. Note intramural portion of common duct (*A*) (arrow).

There is no harm in prolonging the interval between the time telepaque is taken and the time of the examination. Ten to twelve hours later, routine films of the gallbladder are made in the posteroanterior, oblique and upright positions. The ducts are not ordinarily visualized at this time. A fat meal, consisting of two egg yolks in a glass of milk, one-third of which is cream, is then administered in the department. Ten minutes later a film is made in the supine position with the left side elevated about 15 degrees. Routine films are then made at forty minutes at which time the examination is completed, unless additional films seem indicated. All films are inspected by the radiologist immediately after they are processed.

The cystic and common bile ducts are adequately visualized on the ten minute and often on the forty minute film. The hepatic duct is not normally visualized. A higher incidence of duct visualization would be noted if additional films were made at frequent intervals after the the fat meal. If re-examination is desirable for better visualization and further evaluation of the ducts, a dose of 12 tablets (6 grams) may be used.

The bile ducts have been visualized on several occasions in cholecystectomized patients. Further investigation is still needed for standardization of the technique before more uniform results can be obtained.

NORMAL ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

The cystic duct presents a characteristic tortuosity or corkscrew pattern (Fig. 1*C*, 2*C*, 8, 9 and 10), which is produced by the valves of Heister. Its caliber is uniform. The diameter varies between 0.2 and 0.3 cm., as measured on the film. Any appreciable increase in diameter should be considered abnormal and indicative of local dilatation and obstruction (Fig. 7, *A* and *B*).

The cystic duct may join the common bile duct at a right angle or more frequently at an acute angle of varying degrees (Fig. 2, *A* and *B*). In some cases the cystic duct seems to rise practically vertically upwards to join the common duct. The gallbladder then appears as though it were "dangling" or "hanging" (Fig. 1*D*). Figure 2*C* demonstrates an anomaly of the cystic duct. The latter crosses to the left of the common bile duct and then joins it at an acute angle.

The common hepatic bile duct is not visualized during a routine examination. It has a uniform caliber and practically the same diameter as the common bile duct. The latter is uniform in caliber but narrows to a diameter of about 0.1-0.2 cm. at the intramural portion (Fig. 1, *A*, *B* and *C*).

The accepted measurements of the common hepatic and common bile ducts are 0.5–0.7 cm. A study of our cases reveals two sets of measurements. These are 0.2 and 0.5–0.7 cm., respectively. The smaller measurement is most frequently obtained during the early phase of the gallbladder response to a fat meal. At this time the gallbladder is contracting, or in a phase of systole, while bile carrying with it the contrast medium rapidly passes through the common bile duct in a narrow column, or stream, into the duodenum. At this point the sphincter of Oddi is relaxed, or in a phase of diastole. As the gallbladder becomes more and more nearly empty a phase of diastole sets in, the intraductal pressure falls and the sphincter of Oddi is no longer relaxed, but becomes contracted or in a state of systole. At this stage, bile fills the common duct more adequately and a caliber of 0.5 to 0.7 cm. is attained. This normal interaction between the activity of the gallbladder and the sphincter of Oddi is in conformance with, or a manifestation of proper operation of the law of contrary innervation (Fig. 3, *A*, *B*, *C* and *D*).

An imbalance in the function of the gallbladder and the sphincter of Oddi will result in a disturbance of this sequence of contraction and relaxation (Fig. 4, *A* and *B*) (Fig. 5, *A* and *B*). Thus, the gallbladder may be contracting while the sphincter is still contracted, or has failed to relax, and the ducts will remain filled. If the latter is temporary, it would be consistent with an initial spasm of the sphincter of Oddi. A persistent and constant dilatation is indicative of obstruction of varying degrees.

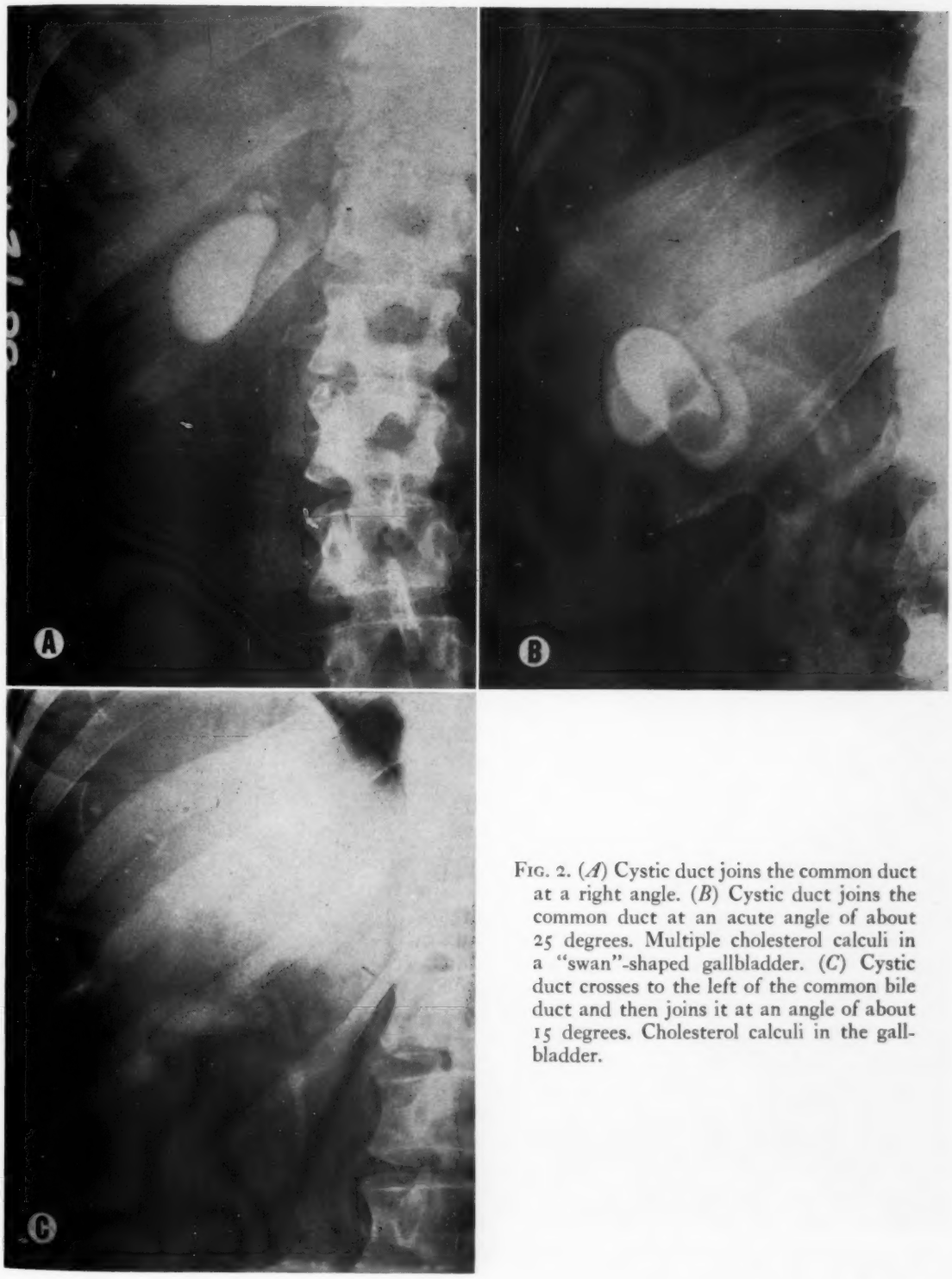


Fig. 2. (*A*) Cystic duct joins the common duct at a right angle. (*B*) Cystic duct joins the common duct at an acute angle of about 25 degrees. Multiple cholesterol calculi in a "swan"-shaped gallbladder. (*C*) Cystic duct crosses to the left of the common bile duct and then joins it at an angle of about 15 degrees. Cholesterol calculi in the gallbladder.

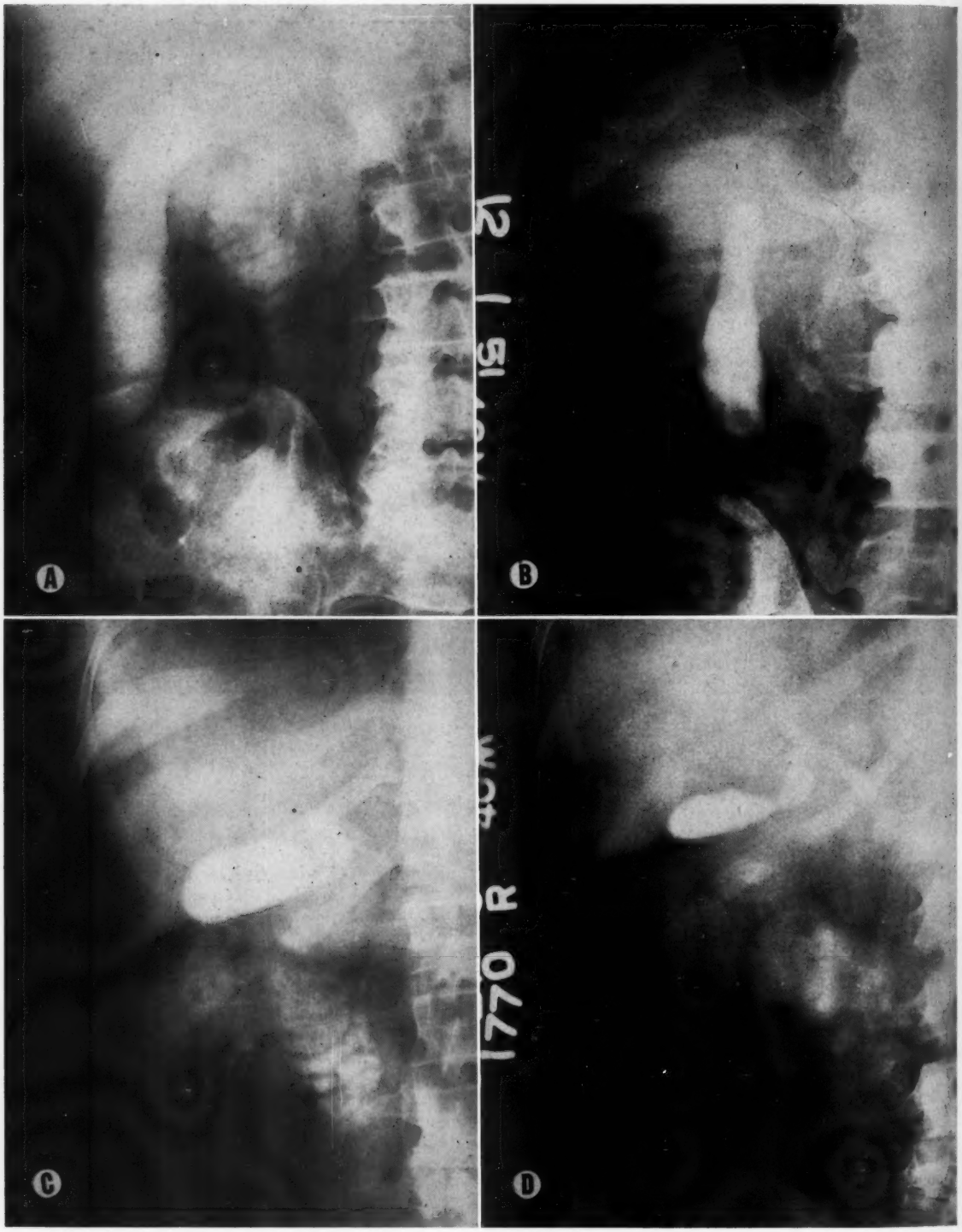


FIG. 3. (*A*) Ten minutes after a fat meal. Common bile duct 0.2 cm. wide. (*B*) Forty minutes after fat meal. common bile duct 0.5 cm. wide.
(*C*) and (*D*) Another case showing similar changes, with some reflux into the hepatic duct.

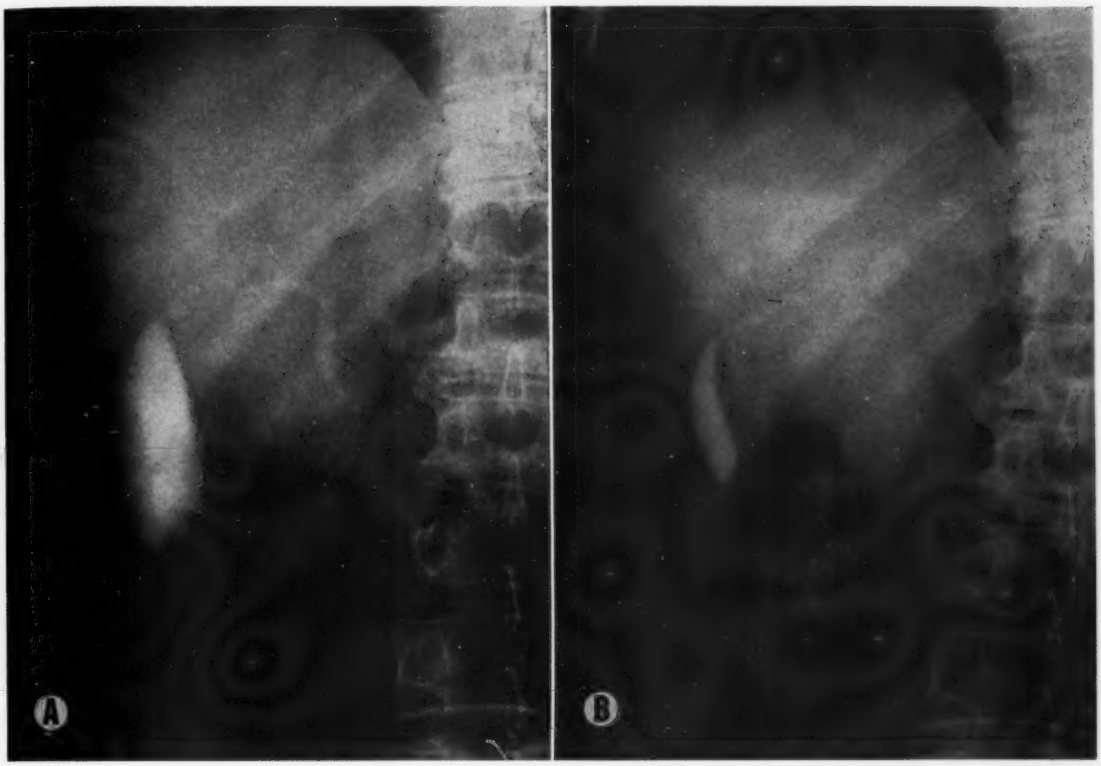


Fig. 4. (*A*) Ten minutes after fat meal. Transitory initial sphincteric spasm with accompanying proximal stasis in distal two-thirds of the common bile duct. Normal cystic duct. (*B*) Forty minutes after fat meal. Spasm has disappeared. There is almost complete emptying of the gallbladder and ducts.

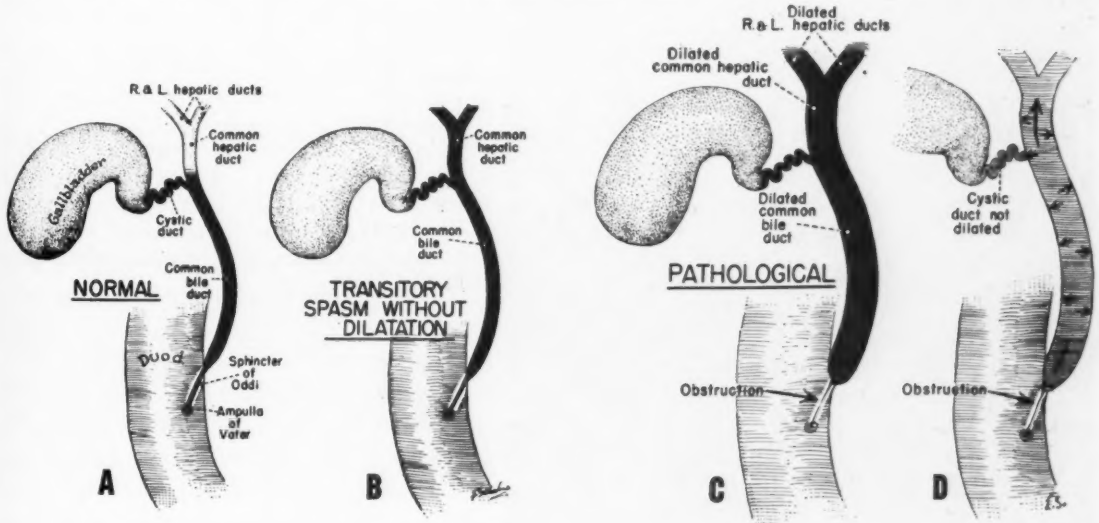


Fig. 5. (*A*) Normal cystic and common bile ducts. The hepatic ducts are not visualized. (*B*) Spasm of the sphincter of Oddi causing reflux and filling the hepatic ducts. The cystic and common bile ducts are visualized, as in (*A*). Note normal caliber of all the ducts. (*C*) Obstruction at the level of the sphincter of Oddi. Dilatation of the hepatic and common bile ducts. Note that the cystic duct remains normal in caliber. (*D*) Diagram showing how "hydraulic" pressure is exerted in all directions, resulting in dilatation of the hepatic and common bile ducts, but not of the cystic duct.

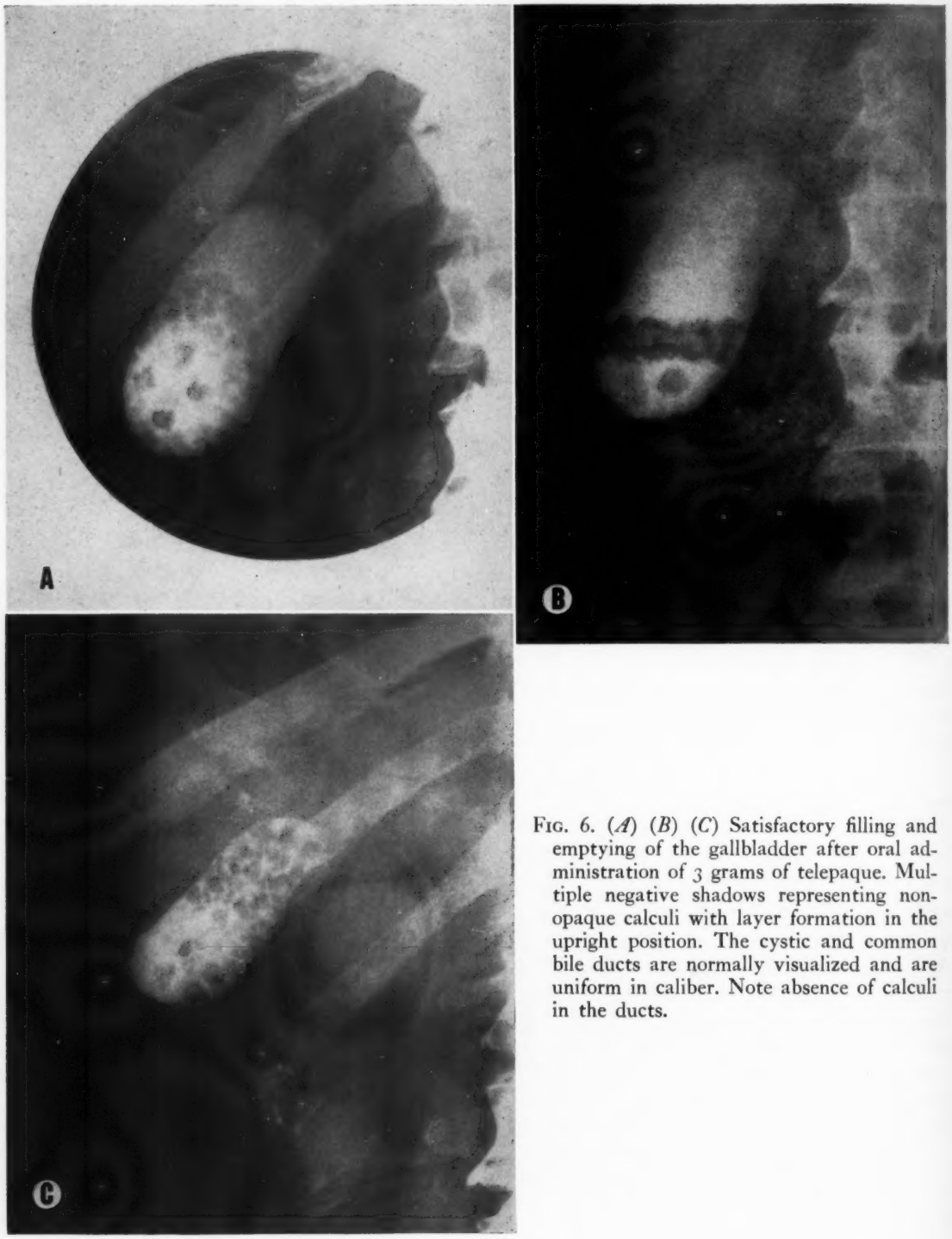


Fig. 6. (*A*) (*B*) (*C*) Satisfactory filling and emptying of the gallbladder after oral administration of 3 grams of telepaque. Multiple negative shadows representing nonopaque calculi with layer formation in the upright position. The cystic and common bile ducts are normally visualized and are uniform in caliber. Note absence of calculi in the ducts.

ABNORMAL ANATOMY AND PHYSIOLOGY

When obstruction occurs at the distal end of the common bile duct, a rise in intraductal pressure follows. This is transmitted uniformly in all directions, horizontally and vertically (Fig. 5, *C* and *D*). The dilatation is uniform, although the lower portion of the common bile duct often appears fusi-

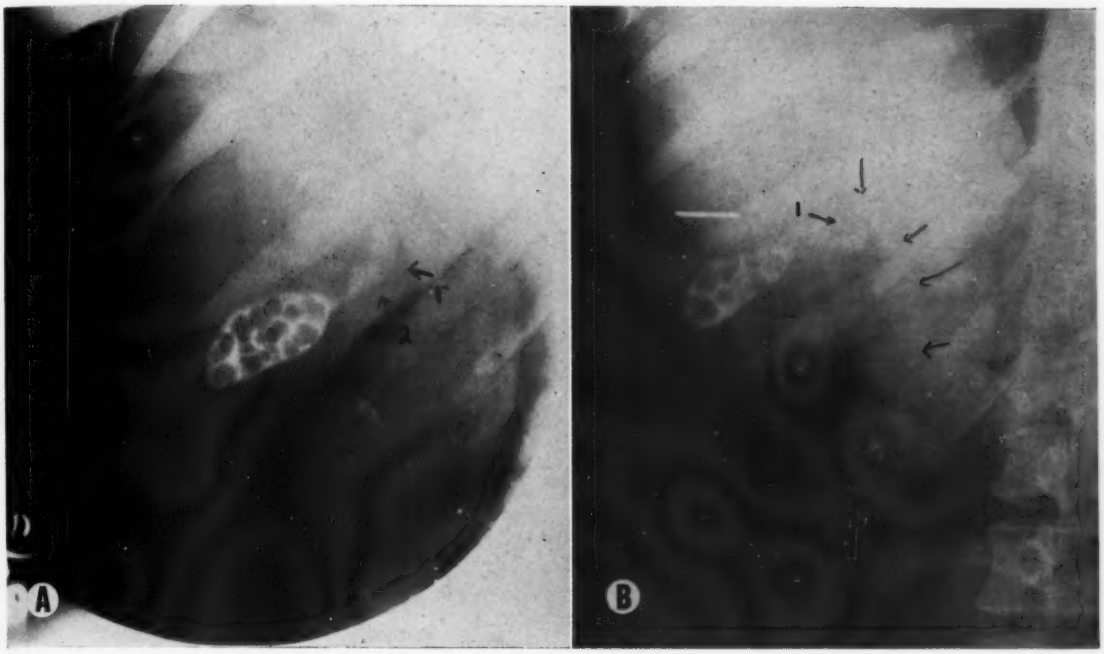


Fig. 7. Case 1. (*A*) Ten minutes after fat meal. Multiple negative shadows representing nonopaque calculi in the gallbladder. Similar shadow in cystic duct (arrow 1) with adjacent dilatation (arrow 2). (*B*) Forty minutes after fat meal. The gallbladder has decreased in size. The cystic duct remains unchanged. The common duct is outlined (better seen on original films).

form or funnel-shaped, unless there are adhesions, pressure or invasion by a new growth, when a defect would be produced. The dilatation progresses upwards to involve the hepatic ducts. It is noteworthy that the cystic duct (Fig. 5, 8 and 9) is not involved in this process and retains its normal caliber. Evidently the complex system of the valves of Heister gives adequate protection against transmission of the increased intraductal pressure into the cystic duct. This function of the valves has perhaps not been adequately appreciated.

In the present state of our knowledge we are justified in considering visualization of the hepatic duct as evidence of obstruction at a point distal to the hepatic duct. This may be temporary when spasm of the sphincter of Oddi occurs and the caliber of of the hepatic duct remains normal (Fig. 5*B*). On the other hand, if fibrosis or muscle hypertrophy of the sphincter occurs, or obstruction due to tumors or other causes sets in, then dilatation of both the common and the hepatic ducts will result (Fig. 5, *C* and *D*).

A high incidence of disturbed duodenal peristalsis, and at times duodenitis, has been observed in association with conditions presenting abnormalities of the sphincter of Oddi and abnormalities and dilatation of the common bile duct. Widening of the duodenal folds extends up to and involves the region of the sphincter of Oddi, but without evidence of a peptic ulcer. The upper gastrointestinal tract should be examined in all cases where the ducts are increased in caliber or where stasis in the ducts is observed. We have often combined our studies of the biliary and gastrointestinal tracts. Barium sulfate is mixed with the fat meal and is administered after the first set of gallbladder films has been made. Unfortunately, some patients seem intolerant of this combination, and varying degrees of initial pylorospasm have been noted. A great deal of caution, therefore, should be exercised in evaluating the pylorospasm so observed. Repetition

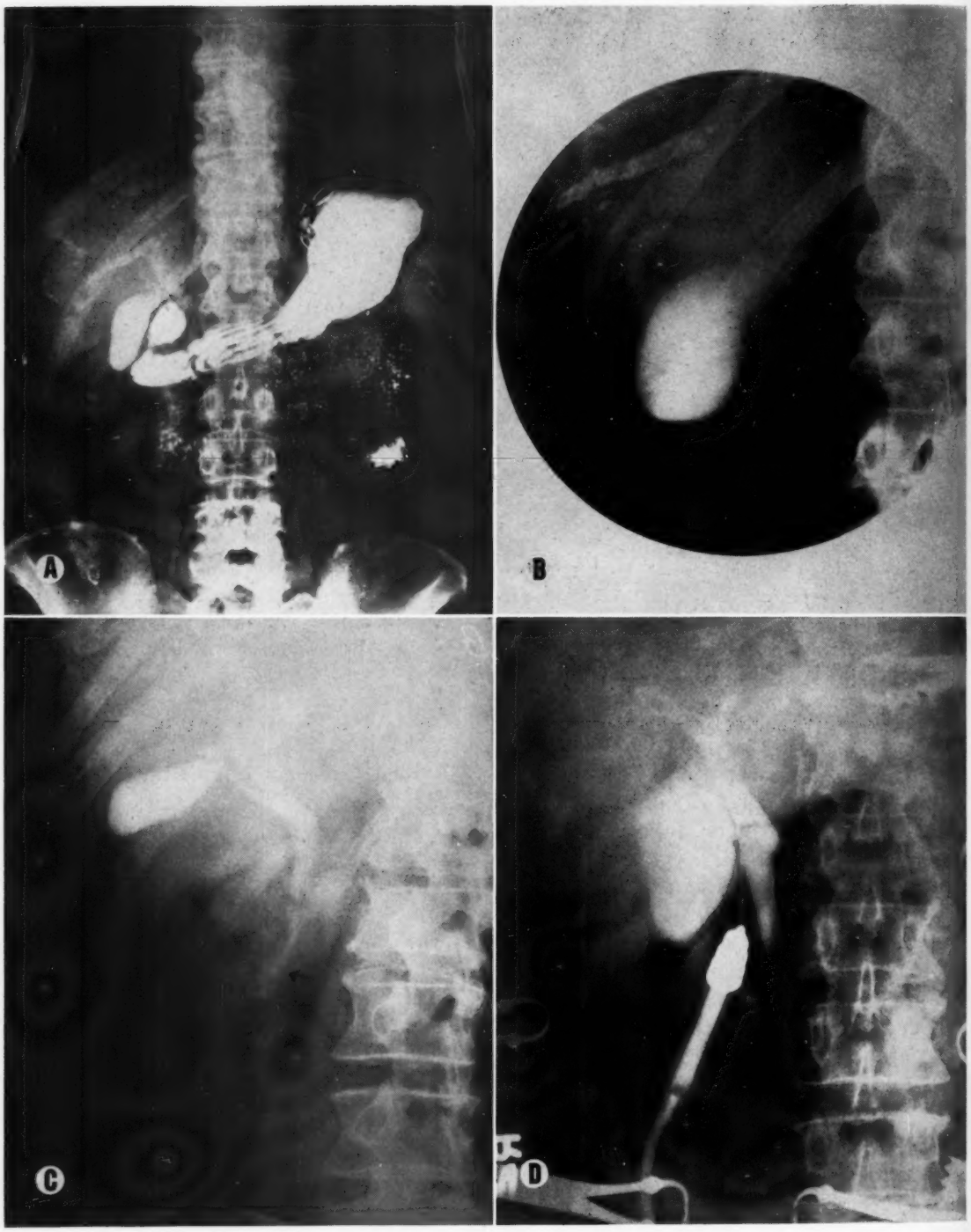
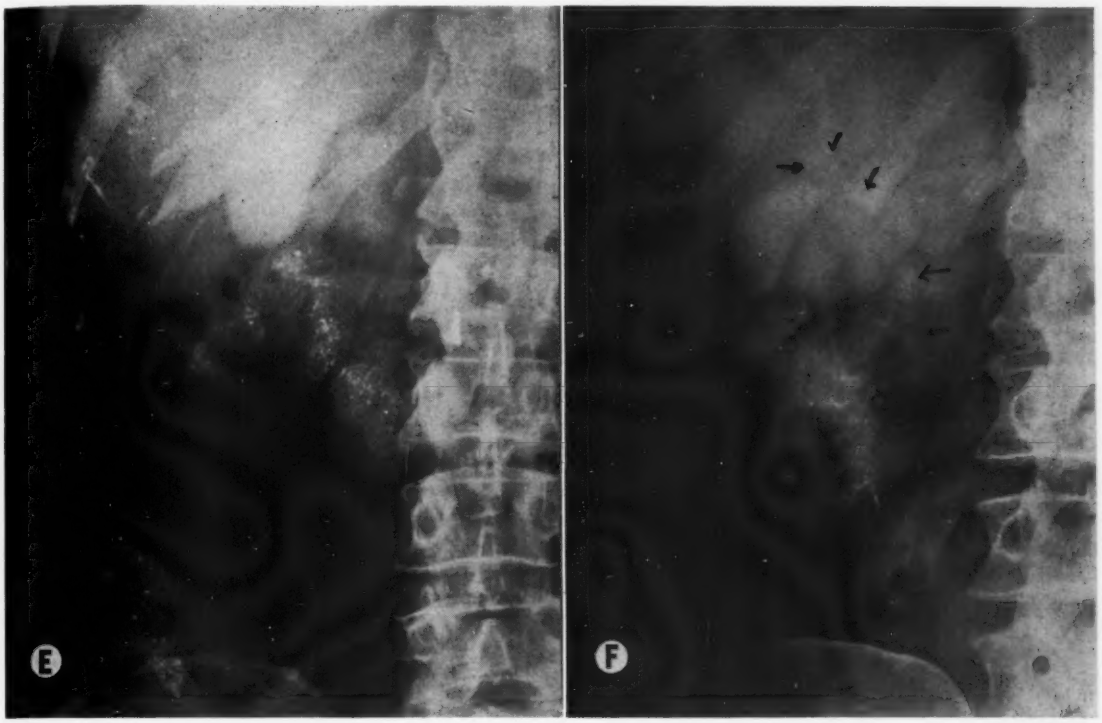


FIG. 8. Case II. (*A*) Combined visualization of the biliary and digestive tracts. Dilated common and hepatic bile ducts, normal cystic duct. Normal gallbladder, stomach and duodenum.

(*B*) Films made twelve hours after administration of 3 grams of telepaque. The hepatic and common bile ducts are dilated.

(*C*) Ten minutes after a fat meal. Size of gallbladder reduced to one-third. The cystic duct is normal. The hepatic and common bile ducts are dilated; the latter is narrow at the intramural portion. Note presence of a minute amount of the contrast medium in the duodenum.

(*D*) Cholangiography in operating room. Ducts appear the same as in (*C*).



(*E*) Cholecystography one month after operation. Film made twelve hours after oral administration of 3 grams of telepaque. The gallbladder is adequately visualized, but no ducts are visualized. Compare with (*A*) and (*B*).

(*F*) Ten minutes after fat meal. The cystic and common bile ducts are visualized. Note that the caliber is normal. The hepatic duct is not visualized. Compare with (*A*) (*B*) and (*C*).

of the examination, with each procedure done separately, often reveals complete absence of the previously noted pylorospasm.

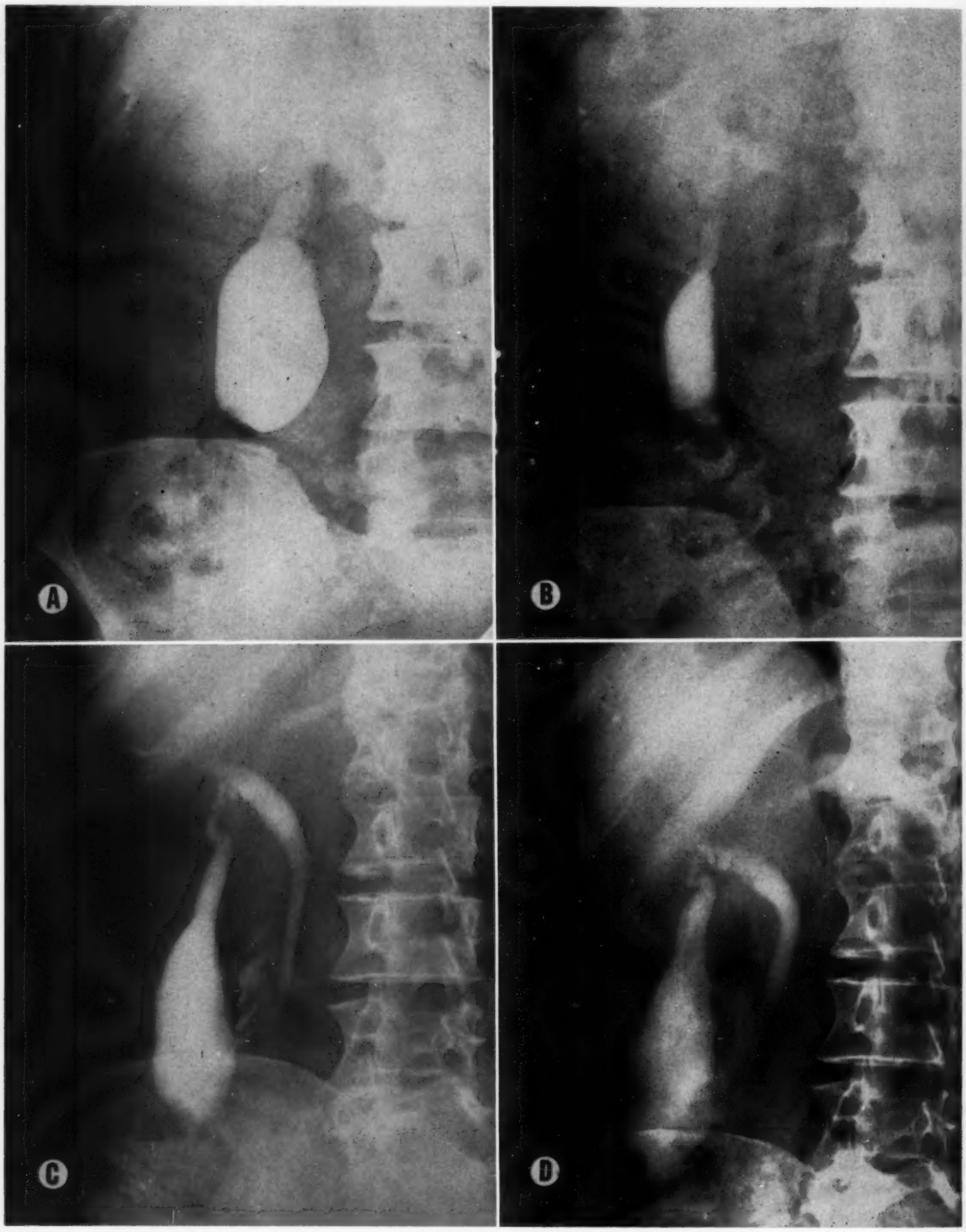
REPORT OF CASES

Case 1. R. F., a white female, aged thirty-two, was admitted to the New York Polyclinic Hospital on March 17, 1952, with the chief complaint of recurrent epigastric and right upper quadrant pain associated with nausea and vomiting, off and on, of five years' duration. Sharp pain is experienced following the intake of meals with a high fat content. Cholecystography following oral administration of 3 grams of telepaque resulted in satisfactory visualization of the gallbladder (Fig. 7, *A* and *B*).

Multiple negative shadows representing numerous nonopaque calculi are noted in the gallbladder. One such shadow is seen in the mid-portion of the cystic duct with adjacent dilatation and accumulation of the contrast medium. The gallbladder decreased in size following the administration of a fat meal but the appearance of the cystic duct remained unchanged.

Cholecystectomy was performed on March 21, 1952. The gallbladder was filled with numerous, rather small cholesterol calculi. One calculus was found in the cystic duct corresponding to the negative shadow indicated by the arrow in Figure 7.

The following three cases had practically identical history and clinical findings. The admission diagnosis in each case was "chronic cholecystitis." These patients complained of varying degrees of epigastric and upper right abdominal pain. There was no history of ulcer-like pains. There was no jaundice. There was a definite intolerance to fatty food and the patients usually felt better on a low fat diet.



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CASE II. H. K., a white housewife, aged forty-five, admitted to the New York Polyclinic Hospital on November 4, 1952. Symptoms were of approximately one year duration. Cholecystography revealed a gallbladder of normal size, shape, density, and reaction to a fat meal. A constant 0.3 cm. defect is noted in the lateral wall of the gallbladder. This was interpreted as

Fig. 9. Case III. (*A*) twelve hours after oral administration of 3 grams of telepaque. Gallbladder well visualized, rather large. Dilated common bile duct is visualized.

(*B*) Prompt response to a fat meal at forty minutes. Gallbladder reduced to about one-fourth its size. The hepatic and common bile ducts are dilated.

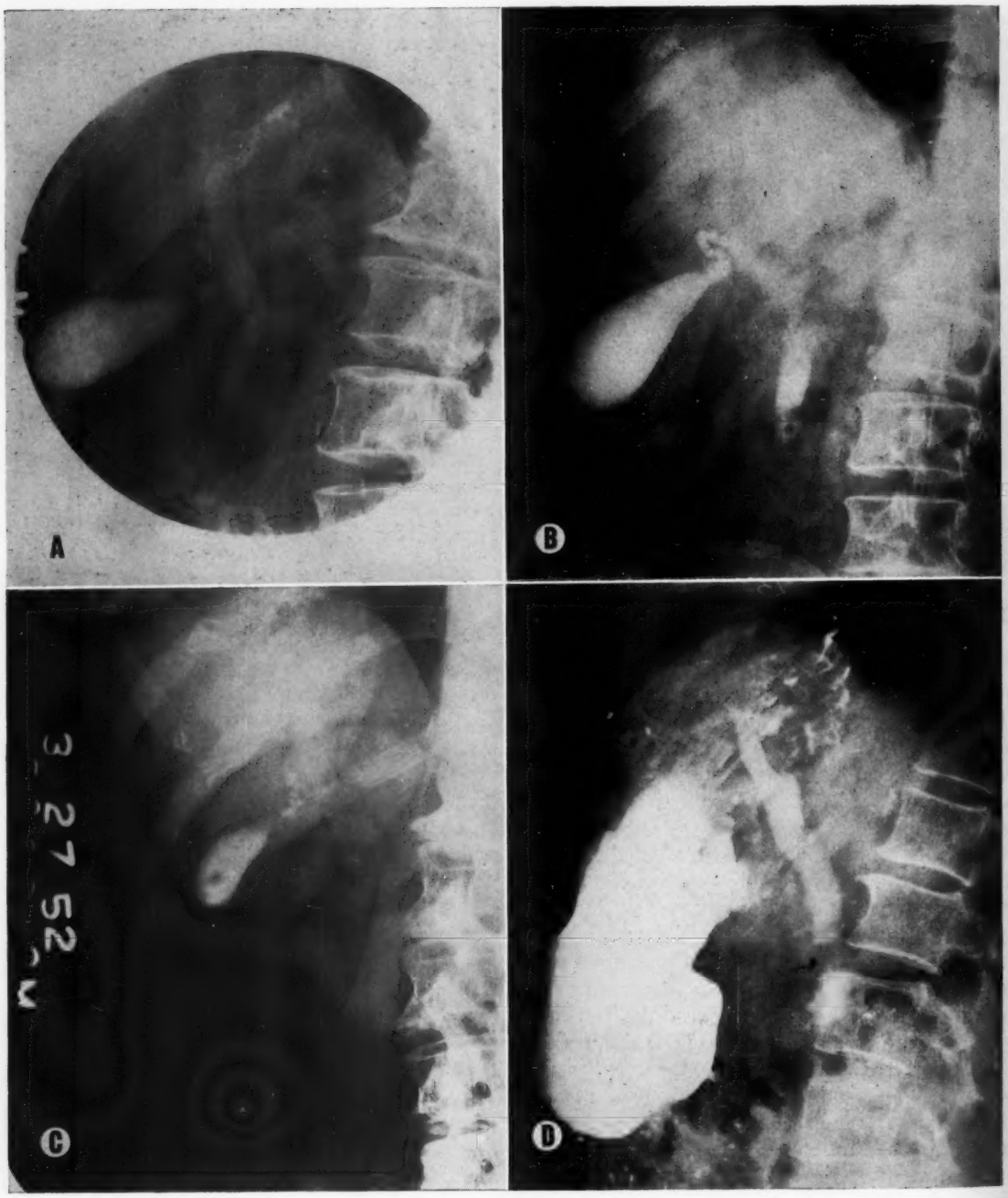
(*C*) Film made ten minutes after fat meal on April 18, 1951. Note straight lower part of common duct and dilatation of upper part, normal caliber of the intramural portion and a small amount of telepaque in the duodenum.

(*D*) and (*E*) Made ten minutes after fat meal on April 4 and October 24, 1952, respectively. Note progressive narrowing of the distal (pancreatic) portion of the common bile duct which has decreased from 0.5 to 0.1 cm.

representing a localized area of cholesterosis. The extrahepatic bile ducts are visualized in their entirety. The cystic duct appears normal while the common hepatic and common bile ducts are dilated. These measured 1.0–1.2 cm. on the film. There was, however, narrowing of the common bile duct at the level of the intramural portion. These findings were confirmed on repetition of the examination with doses of 3 and 6 grams of telepaque, and remained unchanged after administration of belladonna up to the patient's tolerance as well as after administration of nitroglycerine in doses of 1/100 grain. There is no filling defect or deformity. Studies of the gastrointestinal tract revealed considerable irritability of the duodenum without demonstrable intrinsic lesion. The roentgen diagnosis was that of a normal gallbladder function; stenosis at the sphincter of Oddi with incomplete obstruction and dilatation of the common hepatic and common bile ducts (Fig. 8, *A*, *B* and *C*).

At operation the gallbladder appeared normal. There was no palpable mass to correspond to the roentgenologically demonstrable defect in the gallbladder wall. The common hepatic and the common bile ducts were dilated. No calculi could be detected and a search for a tumor mass, intrinsic or extrinsic, in the region of the sphincter of Oddi or distal end of the common bile duct was unsuccessful. Cholangiography in the operating room revealed the same appearance as that observed preoperatively (Fig. 8*D*). The common bile duct was opened. It contained a considerable amount of bile under pressure. A No. 2 and a No. 3 Blake dilator were introduced without great difficulty, but were withdrawn with difficulty. A No. 4 Blake dilator was introduced with great difficulty, passed the sphincter of Oddi into the duodenum, but could not be retracted. Thus an effort to dilate the sphincter, or subsequently cut it through the common duct, was unsuccessful. The duodenum was finally opened. Exploration revealed a considerable thickening of the sphincter and sphincterectomy was performed. A catheter was introduced through the duct into the duodenum, where it was kept for a period of three weeks. The catheter was subsequently removed and the wound completely healed.

Cholecystography (Fig. 8, *E* and *F*) has been performed at monthly intervals. Normal gallbladder function is still maintained, and the ducts are occasionally visualized but are not dilated, indicating ready passage of bile into the duodenum. The patient is still asymptomatic six months after the operation. The prognosis,



(*See opposite page for legend.*)

however, remains guarded as the possibility of recurrence of stenosis cannot be ruled out.

CASE III. S. G., a white female dressmaker, aged fifty-five, was admitted to the New York Polyclinic Hospital on March 26, 1951. Symptoms were approximately of one year duration. The patient had been attending the medical clinic, and cholecystography was performed on several occasions prior to admission. The gallbladder visualized readily after oral administration of 3 grams of telepaque. It appeared to be a little larger than usual, but the response to a fat meal was prompt and adequate (Fig. 9, *A*

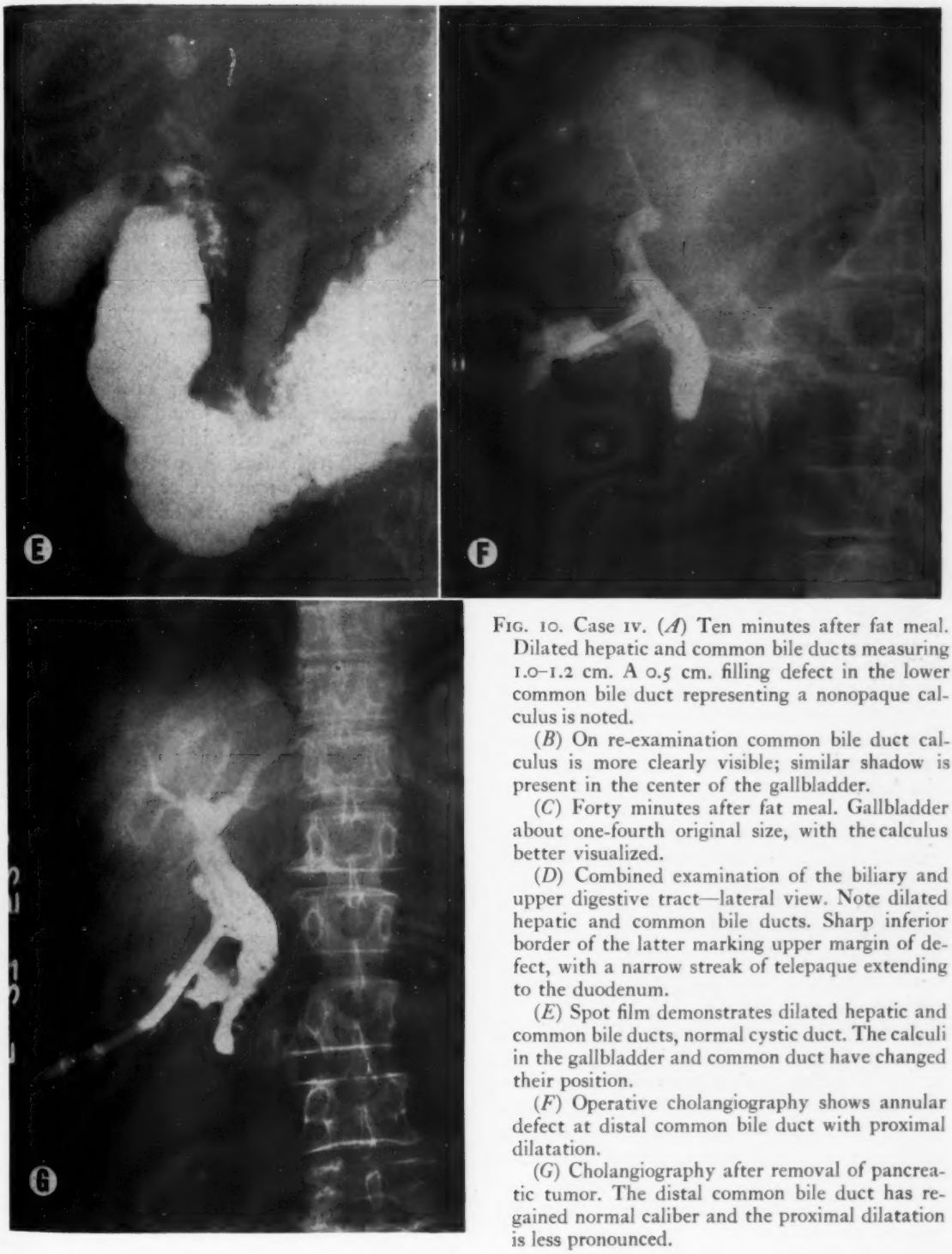


FIG. 10. Case IV. (*A*) Ten minutes after fat meal. Dilated hepatic and common bile ducts measuring 1.0–1.2 cm. A 0.5 cm. filling defect in the lower common bile duct representing a nonopaque calculus is noted.

(*B*) On re-examination common bile duct calculus is more clearly visible; similar shadow is present in the center of the gallbladder.

(*C*) Forty minutes after fat meal. Gallbladder about one-fourth original size, with the calculus better visualized.

(*D*) Combined examination of the biliary and upper digestive tract—lateral view. Note dilated hepatic and common bile ducts. Sharp inferior border of the latter marking upper margin of defect, with a narrow streak of telepaque extending to the duodenum.

(*E*) Spot film demonstrates dilated hepatic and common bile ducts, normal cystic duct. The calculi in the gallbladder and common duct have changed their position.

(*F*) Operative cholangiography shows annular defect at distal common bile duct with proximal dilatation.

(*G*) Cholangiography after removal of pancreatic tumor. The distal common bile duct has regained normal caliber and the proximal dilatation is less pronounced.

and *B*). The common hepatic and proximal portion of the common bile duct are appreciably dilated, measuring from 1.0 to 1.5 cm. in diameter. The distal 2 cm. segment of the common bile duct, however, appears straight and measures about 0.5 cm. in diameter (Fig. 9, *B* and

C). The cystic duct measures 0.3 cm. The findings remained unchanged on repetition of the examination with doses of 6 and 12 tablets of telepaque.

Repeated studies of the stomach and duodenum with a barium meal failed to reveal any evidence of an ulcer or tumor. There was, however, duodenal irritability and during some of the examinations the mucosal folds appeared appreciably wider than normal.

Routine laboratory studies, including complete blood count, blood sedimentation, blood chemistry and routine urine examinations, were within the limits of normal. Cephalin flocculation test was negative and serum amylase was 147 Somogyi units (normal 80 to 150). This rules out acute pancreatitis, which diagnosis was not entertained, but does not rule out chronic pancreatitis.

Roentgen examination of the biliary tract was repeated at an average of six month intervals. This demonstrates progressive narrowing of the distal portion of the common bile duct, which has decreased to a width of approximately 0.1 cm. (Fig. 9, *C*, *D* and *E*).

The patient has refused operation. While surgical confirmation has not been obtained, the findings can best be explained on the basis of a progressive fibrosis of the pancreas, or less likely, of a slowly growing pancreatic tumor encircling the pancreatic portion of the common bile duct.

CASE IV. M. B., a white housewife, aged fifty, was admitted to the New York Polyclinic Hospital on March 27, 1952. The symptoms were of one year duration, with recurrent nausea and vomiting of two months' duration, with exacerbation of abdominal pain. Routine physical examination and laboratory tests failed to reveal any abnormality.

Roentgen studies after oral administration of 3 grams of telepaque revealed the presence of a 0.5 cm. negative shadow representing a solitary nonopaque calculus in an otherwise normal gallbladder. The common hepatic and common bile ducts were considerably dilated, measuring 1.0–1.5 cm. A 0.5 cm. negative shadow is present in the common bile duct representing a nonopaque nonimpacted calculus (Fig. 10, *A*, *B*, *C* and *E*). There is a sharply defined annular defect involving the distal 1.0–1.5 cm. of the common bile duct (Fig. 10*D*). This was considered indicative of an infiltrative neoplastic process of the pancreas causing narrowing and incomplete obstruction of the distal portion of the common bile duct. There was increased gastric and duodenal peristaltic activity, initial pyloric spasm, mushroom-shaped deformity at the base of the duodenal bulb, and widening of the folds of the duodenal mucosa.

Laparotomy was performed on March 31, 1952. The gallbladder contained a small calculus and multiple cholesterol crystals in its wall. The common hepatic and the common bile ducts were dilated and bile was under pressure. Cholangiography in the operating room (Fig. 10*F*) reproduced the previously noted defect at the distal end of the dilated common bile duct. Cholecystectomy was performed. A calculus was found and removed from the common bile duct. The entire pancreas was hard. However, a well defined tumor was found in the head of the pancreas, which extended to the wall of the duodenum. The head of the pancreas, containing the tumor, was removed, part of which had to be dissected from the duodenal wall. Further cholangiography (Fig. 10*G*) demonstrated the disappearance of the defect at the distal end of the common bile duct. The latter regained uniform caliber. The pathologist's report on the resected pancreatic tissue and tumor was (1) acute interstitial pancreatitis, (2) heterotropic pancreatic tissue. The latter had evidently acted as a tumor, encircling the distal portion of the common bile duct.

CONCLUSION

A number of recently made observations on the biliary tract have been presented, perhaps by way of a preliminary report. The bile ducts have been normally visualized and anomalies have been noted. A variety of pathological conditions, which otherwise could not have been demonstrated or diagnosed preoperatively, have also been presented.

Many patients who have had their gallbladders removed because of symptoms ascribed to "cholecystitis" but have retained the same symptoms postoperatively, would fall into one of the groups of cases above presented. With the present method of examination at our command, we should be better prepared to evaluate these cases preoperatively and help the surgeon plan the course he will follow, and, above all, benefit the patient.

It is my sincere hope that an increasing

interest in oral cholangiography will rapidly develop and that a wider concept of the biliary tract, as a whole, and a more inclusive approach to its problems, will quickly displace the hitherto narrow and limiting methods of study of the gallbladder as such.

A great many more questions still have to be answered before this becomes a complete chapter.

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TRAUMATIC HEBERDEN'S NODES

OSTEOARTHRITIS OF THE FINGERS DUE TO INJURY

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HEBERDEN'S nodes are enlargements of the fingers due to osteoarthritis. Two forms have been identified. They arise spontaneously on the fingers of middle-aged women as a hereditary trait, the so-called idiopathic Heberden's nodes. They arise on a finger of a man immediately after a painful injury, the so-called traumatic Heberden's nodes. Idiopathic Heberden's nodes have been carefully studied and accurately described. The present paper aims to describe in some detail the characteristics of traumatic Heberden's nodes and to compare them to idiopathic Heberden's nodes.

Idiopathic Heberden's nodes develop as a hereditary trait, sex-influenced to be dominant in women and recessive in men.[1] Gene frequency analyses indicate a frequency of 70 per cent homozygous normals, 27.2 per cent heterozygotes and 2.7 per cent homozygous recessives. This means that the character affects 2.7 per cent of men and 30 per cent of women. Such proportions occur only at advanced age of the ninth decade when penetrance is complete. The menopause plays some influence, at present unidentified, because Heberden's nodes were noted to appear within three years of the last menstrual period in one-half of the cases.[2] There seems to be no relation between Heberden's nodes and obesity or hypertension.[3] They are a particular form of osteoarthritis, but victims of this disease do not suffer from osteoarthritis of other joints more frequently than a group of people of the same sex and age who do not have Heberden's nodes.[4]

Roentgenologically and clinically, idiopathic Heberden's nodes are due to a localized osteoarthritis of the terminal joints of the fingers.[5] There is no impairment of general health, no alteration in sedimentation rate and no anemia. Roentgenologically there is decreased joint space, irregularity of joint surface, condensation of bone and spur formation. Posteroanterior roentgenograms sometimes seem normal, but proper lateral views show bony spurs arising most commonly from the dorsal aspect of the proximal end of the distal phalanx at the attachment of the extensor tendons, the ventral aspect of the proximal end of the distal phalanx and less frequently at the distal end of the middle phalanx, appearing to be bony extensions of the joint surface. Recently small calcified particles seen in the above locations but not connected to the neighboring bone have been observed. They are often so small as to give no clinical indication of disease, but, seen only in persons who might be genetically susceptible, they are thought to represent poor expressivity of this genetic trait.[6]

Idiopathic Heberden's nodes usually begin as an enlargement of the terminal joint of the index or middle finger of a woman at or near the menopause. The finger is sensitive to pressure or jarring but not really painful and never disabling. In the course of months or years, additional fingers become involved. The sensitiveness usually passes in a few months, but one or two fingers may be painfully involved for as long as five to ten years. As the process progresses, fingers succumb to flexion deformity, and there is later deviation from the straight line.[7] Proximal joints at times are involved. The number of times each individual joint of the finger of both hands was involved in 100 consecutive cases has been presented.[8]

TRAUMATIC HEBERDEN'S NODES

Traumatic Heberden's nodes arise al-

Fig. 1. Case 1. Photograph of the right hand showing enlargement of the distal joint of the forefinger with deviation of the distal phalanx to the ulnar side. The rest of the hand is normal. Posteroanterior roentgenogram of the right forefinger shows displacement and deviation of the distal phalanx to the ulnar side, irregularity of the joint surfaces, decrease in joint space and a bony spur extending proximally from the proximal end of the ulnar side of the distal phalanx.

most immediately in a single finger as the result of an injury. This injury is always a painful one, severe enough to be vividly remembered in all the details for many years. There has been no opportunity as yet to follow the development of this injury from the beginning so this description is obtained by the patients' history. The pain lasts only a few days or weeks, the swelling may subside slightly but after about three months, the finger attains its final state which remains unchanged for the rest of the person's life. In most instances, only one finger is involved, occasionally two adjacent fingers have been injured in the same accident, and very rarely does the victim suffer more than one such injury. The injury is often described as occurring while playing baseball and being hit on the end of the finger. Fingers have been hit with hammers, jammed in automobile doors or closing windows or have been hit against a solid object.

Traumatic Heberden's nodes are very common. One or two examples may be found on every visit to a male medical ward. They do occur, but not so frequently, among women. In a survey of the general population with examination of nearly 7,000 individuals, traumatic Heberden's nodes were found in about 10 per cent of the population. These figures varied with age and cannot be considered as precise. In this study, individual finger enlargement was tabulated for each subject. Subjects with enlargements of at least two fingers on one hand and one finger on the other were arbitrarily counted as having idiopathic Heberden's nodes, the others as traumatic Heberden's nodes.[2]

REPORT OF CASES

Case 1. M. B., a sixty-five year old man with enlargement and deviation to the ulnar side of the distal joint of the right forefinger, shown in Figure 1. The deformity appeared after a baseball injury forty-five years before and has remained unchanged since then. Posteroanterior roentgenogram of the right forefinger shows displacement of the terminal phalanx to the ulnar side, irregularity of the joint space, increased density of bone along the joint line and a large spur, about 3 mm. long, extending proximally from the ulnar side of the proximal surface of the distal phalanx. The rest of the fingers are completely normal.

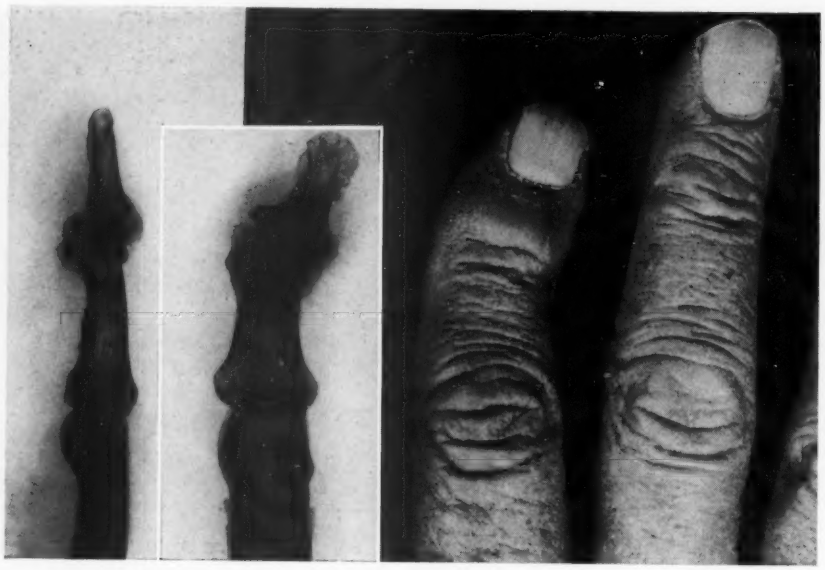

FIG. 2. Case II. Photograph of the forefinger and middle finger of the right hand. The forefinger shows enlargement of the distal interphalangeal joint and deviation to the ulnar side of the distal phalanx. The middle finger is normal. Posteroanterior roentgenogram of the forefinger shows ulnar deviation of the distal phalanx due to the change of direction of the joint surfaces. Lateral view shows an increased amount of bone on the dorsal aspect of the proximal surface of the distal phalanx. The joint space is not seen because of the oblique angle at which the film was taken.

CASE II. F. S., a sixty-eight year old man with enlargement and deviation to the ulnar side of the distal phalanx of the right forefinger, shown in Figure 2. This deformity resulted from a baseball injury forty-eight years ago. The patient states that the condition of his finger has not changed in size or shape since shortly after the injury. The rest of the fingers of the hand are normal. Posteroanterior roentgenogram shows deviation and displacement to the ulnar side without noticeable spur formation. The joint space is irregular, but the joint surfaces seem to be regular. A lateral view shows a massive enlargement of the dorsal aspect of the proximal end of the distal phalanx. The joint space is not seen because of the oblique angle at which the roentgenogram was taken.

CASE III. C. C., a fifty-eight year old man, who shows marked enlargement of the distal joint of the right forefinger shown in Figure 3. This deformity appeared thirty-four years ago when he was hit on the end of the finger while he was playing baseball, and the condition of his finger has not changed since.

Lateral roentgenogram of the index finger shows marked enlargement of the proximal end of the distal phalanx with extension of bone dorsally and ventrally. There is also spur formation on the distal end of the middle phalanx. The joint space is seen only in the dorsal half of the joint. A large ventral spur extends ventrally and proximally.

CASE IV. H. S., a forty-six year old man with enlargement and palmar flexion of the distal joint of the right little finger shown in Figure 4. He injured his finger at work fifteen years before. It became swollen immediately and never returned to its normal, former condition. Posteroanterior roentgenogram was normal, but the lateral view of the fifth finger shows a marked enlargement of the joint surface of the distal phalanx due to an abnormal mass of bone extending dorsally and curving around the joint surface of the middle phalanx. The joint space is regular, and the joint surfaces are smooth.

CASE V. F. M., a forty-five year old man, who shows enlargement of the second and fourth fingers of the right hand. These fingers were injured in a crushing accident about twelve years before. These fingers show a round mass on the dorsum of the distal joints and there is flexion deformity. Posteroanterior roentgenograms are not remarkable, but lateral views show massive,

Fig. 3. Case III. Photograph of the right hand showing marked enlargement of the distal joint of the forefinger with flexion deformity and ulnar deviation. The rest of the fingers are normal. Lateral roentgenogram of the forefinger shows marked increase in bone formation at the proximal end of the distal phalanx with spur formation at the distal end of the middle phalanx. The joint is greatly increased in size, and the joint surfaces and the joint space are well visualized in the dorsal half of the joint. A large mass of bone extends ventrally obscuring the joint space. This is the only instance of this manifestation noted.

bony enlargements extending dorsally from the proximal ends of the distal phalanges of the affected fingers. The joint spaces are normal. The joint surfaces are smooth. The bone structure seems smooth and regular. The third and fifth fingers are included as normals for comparison.

Case VI. D. J., a thirty-four year old man with moderate enlargement of the terminal joints of the third and fourth fingers of the left hand. These enlargements resulted from a kick on the ends of the fingers while playing high school football at the age of seventeen. Roentgenograms of these fingers show marked enlargement of the proximal surface of the distal phalanges with abnormally large masses of bone extending dorsally. The joint surfaces are at least half again as large as normal, they are regular and smooth and the bone structure does not seem to be altered. The joint spaces are normal.

Case VII. A. H., a thirty-four year old man with a small bony mass on the dorsum on the distal joint of the left middle finger. This arose immediately after being struck on the end of the finger with a football. Roentgenogram in the posteroanterior position shows a normal joint. Figure 7 shows a lateral view with marked enlargement of the proximal end of the distal phalanx. Joint surface is about one-half again the normal size, all of the enlargement being due to bone production on the dorsal surface. The joint space is even. The joint surfaces are smooth. The bone structure is not altered.

Case VIII. E. F., a forty-nine year old woman with marked enlargement of the distal phalanx of the left index finger. This deformity appeared shortly after she hurt her hand thirteen years ago. It has remained unchanged since shortly after the accident. Photograph of the second and third fingers (Fig. 8) shows marked enlargement of the distal joint of the index finger, while the third finger is normal. The lateral roentgenogram shows enlargement dorsally of the proximal end of the distal phalanx so that the joint surface is about one and one-half normal size. The joint space is regular and the joint structure is normal. Roentgenogram of the third finger is normal.

Case IX. E. B., a fifty-five year old man with enlargement of the distal joints of the second and fourth fingers of the left hand, resulting from an injury many years ago shown in Figure 9. Lateral roentgenogram shows massive bone production at the proximal end of the distal

FIG. 4. Case IV. Photograph of four fingers of the right hand showing enlargement and flexion deformity of the distal joint of the little finger. Lateral roentgenogram of this finger shows an abnormal mass of bone extending dorsally from the proximal end of the distal phalanx. The joint space is even, the joint surfaces are smooth and the joint area is greatly increased.

phalanx of both of these fingers, resulting in marked increase in the joint surface. The joint spaces are not shown because of the oblique angle at which the roentgenograms were taken. The third and fifth fingers are shown for comparison. Posteroanterior roentgenograms of the fingers of the left hand show marked broadening of the proximal ends of the distal phalanges and of the distal ends of the middle phalanges. There is decrease in joint space but no definite spur formation.

CASE X. W. S., a seventy-two year old man with idiopathic Heberden's nodes of both hands which started to appear at the age of forty-five. He insists, however, that the third finger of the left hand was hurt when he was eighteen years old while playing baseball. The enlargement was apparent at the time of the injury and has not changed in size or shape since several months after injury. Photographs and lateral roentgenograms of four fingers of the left hand seen in Figure 10 show enlargements of all of the terminal joints. Enlargement of the third finger is confined to the dorsal aspect, while enlargements of the other fingers seem to include the ventral aspects also.

Lateral roentgenogram of the third finger shows a large, heavy mass of regular smooth bone extending dorsally from the proximal end of the distal phalanx. The joint surfaces are smooth, the joint space is regular and the distal end of the middle phalanx is normal. These findings seem to be typical of traumatic Heberden's nodes.

Lateral roentgenograms of the second, fourth and fifth fingers show dense, irregular masses of bone extending dorsally and also ventrally from the proximal ends of the distal phalanges, as well as from the distal ends of the middle phalanges. Joint surfaces are rough and irregular, and the joint spaces are narrowed. Irregular, loose bone fragments are seen in the joints. The greater disorganization and irregularity of the bones about the joint seen in idiopathic Heberden's nodes is in marked contrast to the appearance of traumatic Heberden's nodes.

CASE XI. M. C., a seventy-five year old blacksmith who showed enlargements of all the terminal joints of his fingers. He did not remember the circumstances which attended these enlargements.

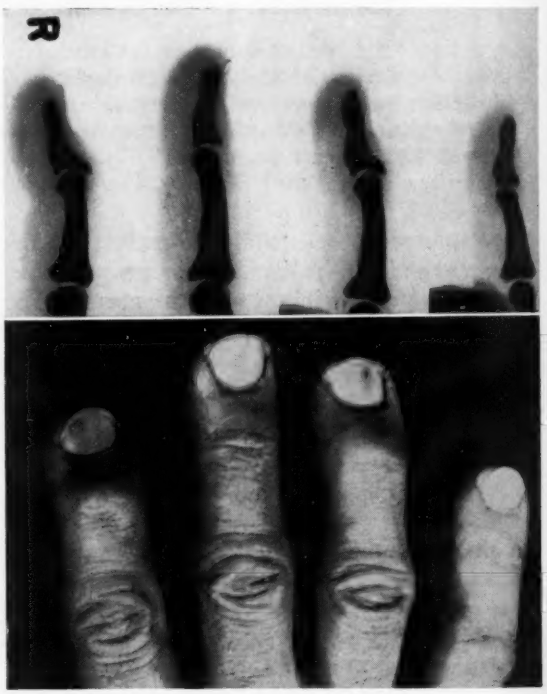

FIG. 5. Photograph of four fingers of the right hand showing flexion deformity and smooth rounded enlargements on the extensor surfaces of the distal joints of the forefinger and the ring finger. The other fingers are normal. Lateral roentgenograms of these fingers show marked contrast between the affected and the normal fingers. The affected fingers show heavy projections of bone extending dorsally from the proximal ends of the distal phalanges producing marked increase in the joint area. The joint spaces are wide, regular and normal, the joint surfaces are smooth, and trabeculation seems to be completely regular and orderly. The distal ends of the middle phalanges are completely normal.

Photograph of four fingers of the right hand seen in Figure 11 shows enlargement of them all, flexion deformity of the forefinger and middle finger and deviation to the radial side of the little finger. Lateral roentgenograms show abnormalities of all terminal joints. In the ring finger these include a large, bony mass extending dorsally and proximally from the proximal end of the distal phalanx. The joint space is even and regular, the joint surfaces are smooth and the distal end of the middle phalanx is normal. These changes are typical of traumatic Heberden's nodes.

The other three fingers show smaller or absent bony projections from the dorsal aspect of the proximal end of the distal phalanges. The joint spaces are not visualized. There are small, pointed bony spurs arising from the dorsal and ventral surfaces of the distal end of the middle phalanges. These changes are in marked contrast to those of traumatic Heberden's nodes

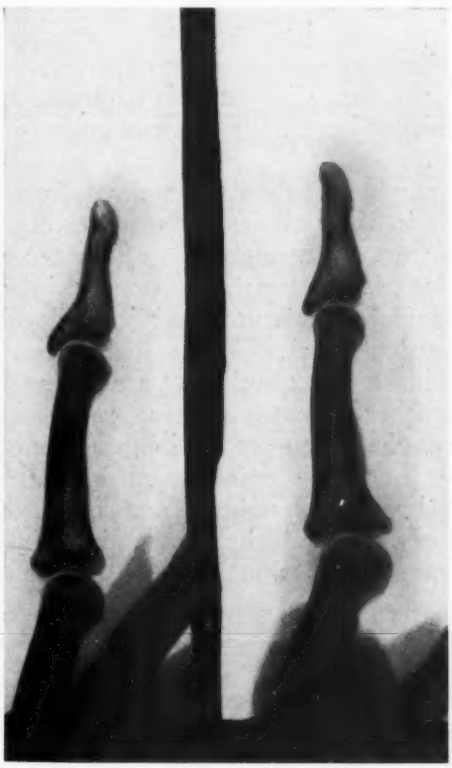

Fig. 6. Lateral roentgenograms of the forefinger and middle finger of the left hand show heavy projections of bone extending dorsally from the proximal ends of the distal phalanges, producing marked increase in the joint area. Joint spaces are regular, joint surfaces are smooth, and bone trabeculation is normal. The middle phalanges are normal.

Fig. 7. Case vii. Lateral roentgenogram of the left middle finger showing very marked increase in size of the proximal end of the distal phalanx, being most marked on the dorsal side. The joint area is increased, the joint space is even, the joint surfaces are smooth and bone trabeculation is normal.

but are often seen in idiopathic Heberden's nodes. In this case, as in Case x, the presence of traumatic Heberden's nodes seemed to prevent the formation of idiopathic Heberden's nodes.

COMMENT

The identification of Heberden's nodes as being of traumatic origin is fairly reliable if the history of the patient and all of the fingers are examined. Occasionally a patient may suffer several accidents with the involvement of mobile fingers. Occasionally adjacent fingers are injured at the same time. By far the largest number of affected persons have only one finger of both hands involved. This comes on as an enlargement after a painful injury and attains a resting stage in several months. This is in striking contrast to the condition relating to idiopathic nodes which begin gradually in one finger, developing slowly over a period of months to several years and spreading from one finger to another without history of injury.

FIG. 8. Case VIII. Photograph of the forefinger and the middle finger of the left hand. The forefinger shows enlargement of the distal joint. The middle finger is normal. Lateral roentgenogram of the forefinger shows marked bony enlargement of the proximal end of the distal phalanx extending dorsally. The joint surfaces and the joint spaces are not well visualized. The distal joint of the middle finger is normal.

After a careful review of photographs of 200 patients with idiopathic Heberden's nodes and comparing with a score or more of cases with traumatic Heberden's nodes, it is seen that certain differences in clinical appearance are common. Despite marked enlargement, deviation of the terminal phalanx of the finger is not nearly so common in traumatic nodes as in Heberden's nodes. To qualify as a Heberden's node the finger must show enlargement. Other defects of the fingers may occur as a result of injury without enlargement but these cannot be classified as Heberden's nodes. Some of them may just be considered as traumatic osteoarthritis. The author recalls a baseball injury occurring to a friend in medical school. After being hit on the end of the finger, the finger showed flexion deformity of the terminal joint. No apparent injury to the joint itself occurred, and extension could be obtained passively. When seen twenty-five years later the patient still had flexion deformity and inability to extend actively the terminal phalanx but without enlargement or deformity of joint and passive extension of the joint.

Traumatic Heberden's nodes differ somewhat in their clinical appearance. Deviation from the straight line of the terminal phalanx is not nearly so common in traumatic Heberden's nodes as it is in idiopathic Heberden's nodes. These deformities are seen in Figures 1 and 2 but are absent from the other 9 cases shown. Enlargement across the dorsum of the joint is characteristic. Since this enlargement is due to a dorsal projection of bone from the proximal end of the distal phalanx, it gives the appearance of a flexion deformity, which may be misleading. The enlargement in some cases appears as a lump highest in the midline and sloping to the sides. In other instances this enlargement extends across the dorsum of the finger as a solid bar. In only one instance was lateral enlargement of the finger known. This is seen in Figure 9. Enlargement of the midline is clearly shown in Figures 5, 9 and 10. Extension across the entire dorsum of the finger is shown in Figures 2, 3, 4, 8, 9 and

11, and was seen also in Cases VI and VII.

Idiopathic Heberden's nodes usually start as enlargements on each side of the midline on the dorsum of the finger as separate nodules. It was this characteristic which gave rise to Heberden's original descriptions starting out as follows:

"What is the nature of the small pea-sized nodules occurring on the back of the finger joints a little to the side? . . ." Even though enlargement does occur across the entire dorsum of the finger in idiopathic nodes, the enlargement is accentuated at the sides. It is true that this characteristic alone may not be sufficient to correctly distinguish the two kinds of Heberden's nodes. Figure 10 shows a traumatic node surrounded on each side by idiopathic nodes for contrast.

The roentgenographic appearance of traumatic Heberden's nodes is best seen in lateral views. Lateral views must be accurately taken to demonstrate the details correctly. The best lateral views in this series are seen in Figures 4, 5, 6, 7, 10 and 11 for traumatic nodes, and Figure 9 for normal fingers. These roentgenograms are correctly taken with the axis of the joint parallel to the direction of the roentgen rays. The two small condyles on the distal end of the middle phalanx are accurately superimposed and a clear view is shown through the joint space with compete separation of the bony elements. When roentgen rays originate proximally to the joint, the joint space is covered up and details are not seen. This is shown in the lateral view of Figures 2, 3 and 9. When roentgen rays originate dorsally or ventrally from the axis of the joint, the lateral lobes of the distal end of the middle phalanx give the appearance of enlargement of the end of the bone both ventrally and dorsally which suggests the presence of spurs. This is shown in Figures 2, 3, 8, 9 and 11.

The changes which seem to be characteristic of traumatic Heberden's nodes are best shown in Figures 4, 5, 6, 7, 10 and 11. A careful study of the problem leads to the assumption that roentgenograms showing these characteristics might well have been obtained with proper care and repeated effort in the other cases. The characteristics noted include a clear and regular joint space, smooth and parallel joint surfaces, absence of deformity at the distal end of the middle phalanx, and enlargement of the proximal end of the

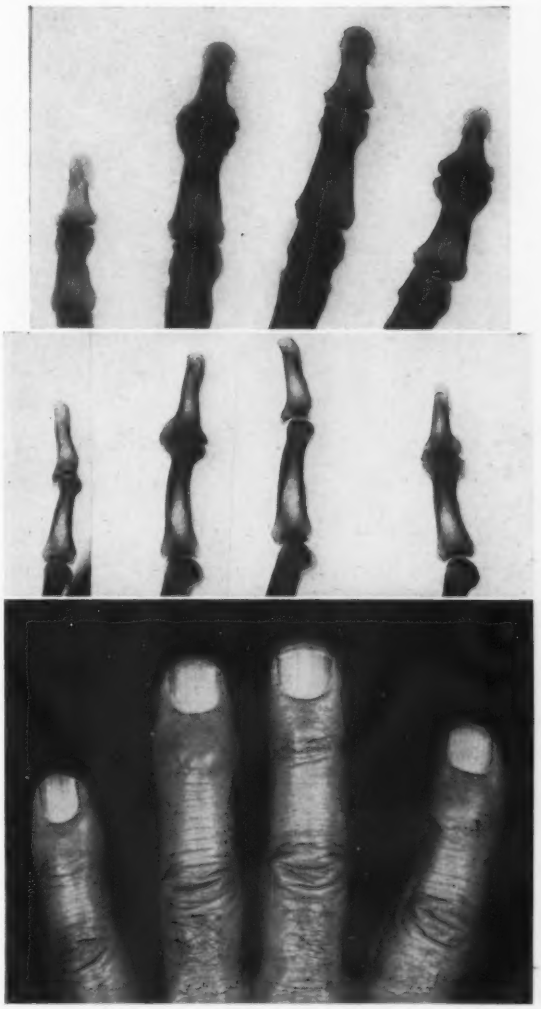

Fig. 9. Case IX. Photograph of four fingers of the left hand showing enlargements dorsally and laterally of the forefinger and ring finger. The other fingers are normal. Lateral roentgenograms show massive bony enlargements of the proximal ends of the distal phalanges of the affected fingers. Joint spaces are not visualized. Posteroanterior views of these fingers show enlargements laterally of the surfaces comprising the distal joint of the affected fingers. Joint spaces are not visualized. The other fingers are normal.

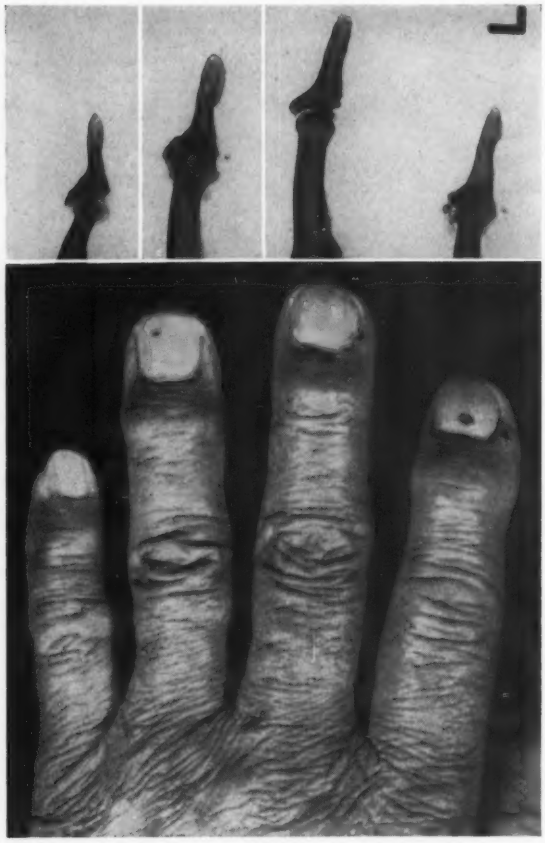

FIG. 10. Case x. Photograph of four fingers of the left hand showing enlargements of all the distal joints. Lateral views of the distal joints show smooth, regular, bony enlargement of the proximal end of the distal phalanx of the middle finger with regular joint space and smooth joint surfaces due to traumatic Heberden's nodes. Joints of the other fingers show irregular bony enlargement of both the distal and the middle phalanges with small detached fragments of bone. These fingers show idiopathic Heberden's nodes.

distal phalanx. Figure 5 shows two traumatic nodes in the same picture with two normal fingers for easy comparison. It is seen that the affected fingers show practically no bony enlargement on the ventral surface. The enlargement on the dorsal surface begins at about the junction of the proximal and middle third of the bone, and the dorsal contour of the bone sweeps dorsally in a smooth even curve, ending at a rather blunt and broad termination. The width of the joint surface of the distal phalanx of these four fingers from left to right is 8, 6, 7 and 6 millimeters. If it were possible to measure the curved surface, it is obvious that this disparity would be even greater. Trabeculations of the bone which were easily seen in the original roentgenograms show normal, even regular arrangement of the bony structure.

Lateral views of idiopathic Heberden's nodes show marked variation from the above description. The joint spaces in idiopathic Heberden's nodes are always reduced and poorly defined. Consequently the joint surfaces are never so clearly distinguishable as has been shown in this series, and when they show anything they show irregularity of the joint surfaces. The bony enlargements often have the appearance of pointed spurs arising from both the dorsal and the ventral surfaces of the proximal end of the distal phalanges and also from both surfaces of the distal end of the middle phalanges. This is seen in the

FIG. 11. Case xi. Photograph of the right hand shows enlargements of all of the terminal joints with flexion deformity of the forefinger and middle finger and deviation of the little finger. Lateral roentgenograms show marked enlargement of the terminal joint of the ring finger due to a large mass of bone projecting dorsally. The other fingers show bony spurs arising from the proximal end of the distal phalanx and the distal end of the middle phalanx.

fourth finger and middle finger of Figure 11.

Traumatic Heberden's nodes differ materially from idiopathic nodes in etiology, speed of development, roentgenographic appearance and usually the subject, although both types of disease may be see in the same hand. Traumatic nodes are the result of a local phenomenon of short duration and they reach their final stage in several months. Idiopathic nodes arise from the general and consitutional stimulus and other manifestations of a long-continuing, slowly developing disease affecting multiple locations in the body. Both conditions are due to osteoarthritis. Pathological study of Heberden's nodes presumably of the idiopathic type shows that there is cartilage degeneration and bone production typical of this disease. The appearance of well taken roentgenographic traumatic nodes gives little indication of cartilage degeneration or cartilage disappearance. There is furthermore no roentgenographic evidence of alteration in intimate bone architecture, but only alteration of the gross shape.

The exact nature of the injury giving rise to traumatic Heberden's nodes is not known. It is thought that baseball injuries might give rise to a sprain with separation of some of the fibers of the extensor tendons and the attachments to the base of the distal phalanx. Such stretching, distortion and displacement of the tendons might give rise to bone production as it does on the borders of vertebral bodies near the intervertebral discs with the production of spurs. It seems unlikely that fracture to the tendinous attachments of the fingers would heal without leaving more evidence of callous formation. Further information on these details might be obtained from careful study and serial roentgenographic examination of fingers beginning immediately upon injury. If such studies have been reported, they are unknown to the authors.

Traumatic Heberden's nodes not only differ materially from idiopathic Heberden's nodes but they seem to protect the fingers from idiopathic Heberden's nodes. In Cases x and xi it is shown that injured fingers developed no evidence of the characteristics of idiopathic nodes although all the other fingers of the hand were involved.

CONCLUSIONS

1. Traumatic Heberden's nodes are enlargements of the terminal joints of the fingers resulting from injury.

2. The injury is usually severe enough to be remembered, it results in immediate deformity, and it reaches a resting stage in about three months.

3. The clinical appearance of Heberden's nodes is different from that usually seen in idiopathic Heberden's nodes.

4. The roentgenographic appearance of Heberden's nodes differs materially from that of idiopathic Heberden's nodes.

5. It appears that fingers affected with traumatic Heberden's nodes are immune to the changes of idiopathic Heberden's nodes.

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SOME OBSERVATIONS CONCERNED WITH CARCINOMA OF THE BREAST*

PART II

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DURING the years 1923 to 1943, 1,034 patients with carcinoma of the breast were seen at the Hospital of the University of Pennsylvania.[1,2,3] In Part I of this present study[6] these patients have been classified into various categories in order that our experience might be compared with that of others.

OUTLINE OF RADIATION TREATMENT

Tables XII, XIII and XIV‡ represent an effort to catalogue the type of treatment received by a patient and the number of five year survivals. It is worthy of note that numerous patients received radiation treatment for recurrences and metastases in addition to their primary irradiation, preoperative irradiation, etc. Under the heading of Operation and Irradiation for recurrences and metastases in the above three tables we include patients who received such radiation as their only form of radiation therapy.

Of the 919 patients, referred to in Tables XII and XIII, 362 had operation only, 24 had preoperative irradiation, 34 had both pre-

* From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, and the Penn Mutual Life Insurance Foundation for the Study of Neoplastic Diseases, and supported in part by the Institutional Grant of the American Cancer Society.

† Clinical Fellow of the American Cancer Society.

‡ Richards' Clinical Index of Malignancy, Carcinoma of Breast.[5]

	Weighting Factor	Gradation Factor	
Lactation	L-1	Absent	0
		Present	9
Age	A-2	Prior to menopause	1
		Four years or more after menopause	2
		Concurrent with or up to four years after menopause	4
Site	S-3	Outer quadrant without nodes	½
		Inner quadrant without nodes	2
		Outer quadrant with nodes	3
		Inner quadrant with nodes	5
Rate of growth	R-4	Slow	1
		Moderate	2
		Fast	3
		Rapid (Inflammatory)	4
Stage or extent	E-5	†Stage I	1
		Stage II	2
		Stage III	3
		Stage IV	4
		Stage V	5

The clinical index in any case equals the lactation factor, plus twice the age factor, plus three times the site factor, plus four times rate of growth, plus five times the factor for stage or extent. Thus:

$$C.I.M. = 1L + 2A + 3S + 4R + 5E$$

When the total adds up to 10 to 30, the degree of malignancy is low and the prognosis will be good. Operative therapy is indicated in this group. When the total adds up to 31 to 40, the degree of malignancy is intermediate; when the total is higher than 40, the degree of malignancy is high and the prognosis is extremely unfavorable. Operative therapy is at least undesirable and is usually contraindicated.

† For definition of stages (Richards' Mammary Carcinoma by Stage of Disease—see Part I[6]).

TABLE XII

NUMBER AND PERCENTAGE OF 5 YEAR SURVIVALS BY PORTMANN'S CLINICAL CLASSIFICATION CONSIDERING OPERATION ONLY (362 CASES) AND OPERATION PLUS IRRADIATION (557 CASES) (CARCINOMA OF BREAST)

Classification Group	No. of Cases	Operation Only			Preoperative Irradiation Alone			Preoperative and Postoperative Irradiation			Postoperative Irradiation Alone			Postoperative Prophylactic Irradiation			Operation and Irradiation for Recurrences or Metastases			Unclassified Irradiation and Operation		
		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
I	479	212	148	69.8	10	2	20.0	11	6	54.5	158	71	45.1	10	5	50.0	75	30	40.0	3	0	0
II	267	90	24	26.7	6	2	33.3	9	2	22.2	97	26	26.8	10	6	60.0	54	11	20.3	1	0	0
III	80	25	7	28.0	6	1	16.6	2	1	50.0	26	6	23.0	2	1	50.0	16	3	18.7	3	0	0
IV	56	23	1	4.3	2	0	0	9	0	0	9	0	0	1	0	0	9	2	22.2	3	0	0
Unclassified	37	12	0	0	0	0	0	3	1	33.3	13	3	23.0	6	0	0	3	1	33.3	0	0	0
TOTALS	919	362	180	49.7	24	5	20.8	34	10	29.4	303	106	34.9	29	12	41.3	157	47	29.9	10	0	0

operative and postoperative irradiation, 303 had postoperative irradiation (to the operative field), 29 had postoperative prophylactic irradiation (to other sites than the operative field), 157 had irradiation for recurrences or metastases following operation and 10 others had unclassified irradiation with operation. In addition, some of these patients had preoperative or postoperative castration and that particular subject will be considered in a subsequent report.

Our five year survival data on the various categories of irradiation and operation show no increased survival of the irradiation group over that obtained by operation alone. However, here and there in the tables, one may observe in the *various stages or groups* an apparent percentage advantage of one combination of radiation treatment compared with another form of radiation treatment. It is not known whether this observation is significant or not because of: (1) the small number of cases, or (2) the effect of the operation itself.

Richards[5] in 1948 stated: "It may, therefore, reasonably be doubted whether much more is to be expected as a result of improvements in surgical therapy *alone* than is at present being accomplished. Obviously, also, the results which may be achieved by surgical methods provide the criterion against which all other methods must be measured. It is upon a comparison with surgical results that we must finally decide whether any suggestions put forward as improvements are valid or otherwise." In Richards' series of 1,271 cases, irradiation when combined with operation was more effective than operation alone.

In an attempt to compare our results with those of Richards, we classified our cases according to his methods, using

TABLE XIII

NUMBER AND PERCENTAGE OF 5 YEAR SURVIVALS BY RICHARDS' STAGE OF DISEASE CLASSIFICATION CONSIDERING OPERATION ONLY (362 CASES) AND OPERATION PLUS IRRADIATION (557 CASES) (CARCINOMA OF BREAST)

Classification Stage	No. of Cases	Operation Only			Preoperative Irradiation Alone			Preoperative and Postoperative Irradiation			Postoperative Irradiation Alone			Postoperative Prophylactic Irradiation			Operation and Irradiation for Recurrences or Metastases			Unclassified Irradiation and Operation		
		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.		No.	5 yr. surv.	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
I	120	66	58	87.8	0	0	0	1	1	100.0	29	21	72.4	3	2	66.6	18	13	72.2	3	0	0
II	169	55	30	54.5	0	0	0	5	2	40.0	64	30	46.8	5	3	60.0	40	16	40.0	0	0	0
III	304	128	71	55.4	9	3	33.3	9	3	33.3	105	35	33.3	7	5	71.4	40	13	32.7	6	0	0
IV	212	71	20	28.1	11	2	18.1	9	3	33.3	76	19	25.0	7	0	0	38	3	7.8	0	0	0
V	74	28	1	3.6	3	0	0	9	0	0	17	0	0	2	1	50.0	14	1	7.1	1	0	0
Unclassified	40	14	0	0	1	0	0	1	1	100.0	12	1	8.3	5	1	20.0	7	1	14.2	0	0	0
TOTALS	919	362	180	49.7	24	5	20.8	34	10	29.4	303	106	34.9	29	12	41.3	157	47	29.9	10	0	0

tables similar to his, and our results are presented in Tables XIII and XIV. It is to be seen from our data that there was no significant improvement in our five year survival rates by the addition of irradiation to operation.

Table XV indicates that the more undifferentiated a breast tumor inclines to be, the less the five year survival, stage by stage, treatment by treatment.

Portmann[4] in 1943 stated he applied his Four Group Classification to a series of 1,000 cases of cancer of the breast and his data showed that there was a percentage gain when irradiation was combined with operation in Groups II, III and IV. We have attempted to compare Portmann's series and ours, and the results are shown in Table XVI.

Twenty-four patients were given preoperative irradiation alone. These cases were analyzed carefully and no significant trend was noted as to whether irradiation, when given prior to operation, contributed anything to longer survival.

Tables XII, XIII, and XIV show that 34 patients had preoperative and postoperative irradiation. Of these, 10 lived for five years. For the most part, these patients were in the advanced stages of their disease.

There were 303 patients who received postoperative irradiation without preoperative irradiation. Of these, 106 survived five years or longer (Tables XII, XIII and XIV). Of these 303 patients who had postoperative irradiation, 226 had it to the operative field and axilla, 48 had it to the operative field only, 23 had it to the axilla only, and in 6 the details were not coded.

Tables XVII, XVIII and XIX refer to the 226 cases in the above group who had postoperative irradiation to the operative field and axilla and to the 48 who had it to the operative field only (total 274 cases). It will be observed that 244 of these 274 patients received 3,000 r or less tumor dose at all stages of disease. An analysis of the effect of time after operation when irradiation was begun for these 274 patients is presented in Tables XX and XXI. We are

TABLE XIV

NUMBER AND PERCENTAGE OF 5 YEAR SURVIVALS BY RICHARDS' CLINICAL INDEX OF MALIGNANCY CONSIDERING ALL CODED PATIENTS (CARCINOMA OF BREAST)

C.I.M. Degree of Malignancy	Total Coded Cases	Operation Only			Preoperative Irradiation Alone			Preoperative and Postoperative Irradiation			Postoperative Irradiation Alone			Postoperative Prophylactic Irradiation			Operation and Irradiation for Recurrences or Metastases			Unclassified Irradiation and Operation			Irradiation Only			Survival or Non-survival Unknown, Considered as Dead (Cases)		
		Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Total No.	5 yr. surv. No.	5 yr. surv. Per cent	Operation	Operation and Irradiation	Irradiation
10–30	271	132	101	76.5	1	0	0	5	3	60.0	79	45	56.9	6	5	83.3	40	21	52.5	3	0	0	5	1	20.0	9	8	1
31–40	337	120	59	46.1	11	4	36.3	14	6	38.5	100	36	33.0	7	2	28.5	53	17	32.0	6	0	0	17	2	11.7	20	9	5
Over 40	366	97	14	14.4	12	1	8.3	14	0	0	93	19	20.4	10	3	30.0	54	7	12.9	1	0	0	85	2	2.3	53	54	54
Unclassified	55	13	6	46.1	0	0	0	1	1	100.0	22	6	45.0	6	2	33.3	10	2	20.0	0	0	0	3	1	33.3	3	3	1
TOTALS	1,029	362	180	49.7	24	5	20.8	34	10	29.4	303	106	34.9	29	12	41.3	157	47	29.9	10	0	0	110	6	5.4	85	74	61

Note: This table is arranged similar to Table XII on page 118 of Richards' article—Mammary cancer; the place of surgery and of radiotherapy in its management. *Brit. J. Radiol.*, 1948, *21*, 109–127.

TABLE XV

CORRELATION OF OPERATION ONLY AND OPERATION PLUS IRRADIATION (PORTMANN'S GROUP CLASSIFICATION) WITH DEGREE OF MICROSCOPIC DIFFERENTIATION OF TUMOR AND 5 YEAR SURVIVALS (CARCINOMA OF BREAST)

Classification	Operation Only									Operation plus Irradiation								
Group	No. of Cases	*D*	5 yr. *S*	*M*	5 yr. *S*	*U*	5 yr. *S*	*N*	5 yr. *S*	No. of Cases	*D*	5 yr. *S*	*M*	5 yr. *S*	*U*	5 yr. *S*	*N*	5yr. *S*
I	212	6	6	107	85	93	51	6	6	267	12	10	91	54	113	36	51	14
II	90	5	3	25	7	52	7	8	7	177	2	2	47	16	88	19	40	10
III	25	0	0	9	5	12	4	4	0	55	0	0	12	6	23	3	20	3
IV	23	0	0	5	1	9	0	9	0	33	0	0	4	0	17	0	12	2
Unclassified	12	0	0	0	0	0	0	12	0	25	0	0	0	0	0	0	25	5
TOTALS	362	11	9	146	96	166	62	39	13	557	14	12	154	76	241	58	148	34

Code: *D* = well differentiatiated tumor; *M* = moderately well differentiated tumor; *U* = undifferentiated tumor; *N* = differentiation of tumor unknown; 5 yr. *S* = 5 year survival.

TABLE XVI

COMPARISON OF PORTMANN'S[4] AND UNVIERSITY OF PENNSYLVANIA'S CARCINOMA OF BREAST PATIENTS BASED ON PERCENTAGES, INCIDENCE OF EACH GROUP AND 5 YEAR SURVIVAL RATES

Classification	Portmann (1,000 Cases)			University of Pennsylvania (919 Cases)		
Group	Incidence	5 year survival rates		Incidence	5 year survival rates	
		Operation	Operation plus Irradiation		Operation	Operation plus Irradiation
	(per cent)	(per cent)	(per cent)	(per cent)	(per cent)	(per cent)
I	25	90	90	52	69.8	42.7
II	25	50	65	29	26.7	26.6
III	30	5	15	8	28.0	21.8
IV	20	5	10	6	4.3	6.1
Unclassified	0	0	0	4	0	20.0

TABLE XVII

POSTOPERATIVE IRRADIATION. EFFECT ON 5 YEAR SURVIVAL BY VARIOUS TUMOR DOSES OF RADIATION ACCORDING TO PORTMANN'S FOUR GROUP CLINICAL CLASSIFICATION

Tumor Dose in Roentgens	No. of Cases	Group I			Group II			Group III			Group IV			Group not Coded		
		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
50–499	25	9	2	22.2	10	1	10.0	4	0	0	1	0	0	1	1	100.0
500–1,499	137	79	42	53.1	42	14	33.3	8	1	12.5	5	0	0	3	2	66.6
1,500–2,999	82	35	17	48.5	33	7	21.2	8	4	50.0	2	0	0	4	0	0
3,000–3,999	11	7	2	28.5	1	0	0	2	0	0	0	0	0	1	0	0
4,000–4,999	5	3	1	33.3	1	0	0	0	0	0	0	0	0	1	0	0
5,000–5,999	2	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Over 6,000	3	2	0	0	1	1	100.0	0	0	0	0	0	0	0	0	0
Not coded	9	6	2	33.3	2	1	50.0	1	0	0	0	0	0	0	0	0
TOTALS	274	142	66	46.4	90	24	26.6	24	5	20.8	8	0	0	10	3	30.0

Note: This table includes only those patients receiving postoperative irradiation to the chest. Of the 303 patients receiving postoperative irradiation (see Tables XII, XIII and XIV) there were 226 to the operative field and axilla, 48 to the operative field only, 23 to the axilla only and 6 others the details of which are unknown.

TABLE XVIII

POSTOPERATIVE IRRADIATION EFFECT ON 5 YEAR SURVIVAL BY VARIOUS TUMOR DOSES OF IRRADIATION ACCORDING TO RICHARDS' FIVE STAGE OF DISEASE CLASSIFICATION

Tumor Dose in Roentgens	No. Cases	Stage I			Stage II			Stage III			Stage IV			Stage V			Stage not Coded		
		Cases treated	5 yr. surv.		Cases treated	5 yr. surv.		Cases treated	5 yr. surv.		Cases treated	5 yr. surv.		Cases treated	5 yr. surv.		Cases treated	5 yr. surv.	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
50–499	25	1	0	0	6	3	50.0	10	1	10.0	6	0	0	2	0	0	0	0	0
500–1,499	137	19	13	68.2	30	16	53.3	40	18	45.0	33	9	27.2	9	0	0	6	3	50.0
1,500–2,999	82	7	4	57.1	17	7	41.1	31	8	25.8	18	7	38.8	5	0	0	4	2	50.0
3,000–3,999	11	1	1	100.0	3	1	33.3	2	0	0	4	0	0	0	0	0	1	0	0
4,000–4,999	5	0	0	0	2	0	0	3	1	33.3	0	0	0	0	0	0	0	0	0
5,000–5,999	2	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0
Over 6,000	3	0	0	0	1	0	0	1	1	100.0	1	0	0	0	0	0	0	0	0
Not coded	9	1	1	100.0	0	0	0	6	2	33.3	2	0	0	0	0	0	0	0	0
TOTALS	274	29	19	65.5	59	27	45.7	94	31	32.9	65	16	24.6	16	0	0	11	5	45.4

Note: This table includes only those patients receiving postoperative irradiation to the chest. Of the 303 patients receiving postoperative irradiation (see Tables XII, XIII, XIV) there were 226 to the operative field and axilla, 48 to the operative field only, 23 to the axilla and 6 others the details of which are unknown.

TABLE XIX

POSTOPERATIVE IRRADIATION. EFFECT ON 5 YEAR SURVIVAL BY VARIOUS TUMOR DOSES OF RADIATION ACCORDING TO RICHARDS' CLINICAL INDEX OF MALIGNANCY CLASSIFICATION (CARCINOMA OF BREAST)

Tumor Dose in Roentgens	No. of Cases	C.I.M. 10 to 30			C.I.M. 31 to 40			C.I.M. over 40			C.I.M. not coded		
		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
50–499	25	5	2	40.0	8	2	25.0	12	0	0	0	0	0
500–1,499	137	40	26	65.0	48	20	41.7	40	9	22.5	9	4	44.4
1,500–2,999	82	24	12	50.0	28	8	28.5	25	6	25.0	5	2	40.0
3,000–3,999	11	4	2	50.0	3	0	0	3	0	0	1	0	0
4,000–4,999	5	0	0	0	3	1	33.3	0	0	0	2	0	0
5,000–5,999	2	0	0	0	1	0	0	1	0	0	0	0	0
Over 6,000	3	1	1	100.0	1	0	0	1	0	0	0	0	0
Not coded	9	1	1	100.0	4	1	25.0	4	1	25.0	0	0	0
TOTALS	274	75	44	58.6	96	32	33.3	86	16	18.6	17	6	35.2

Note: This table includes only those patients receiving postoperative irradiation to the chest. Of the 303 patients receiving postoperative irradiation (see Tables XII, XIII, XIV) there were 226 to the operative field and axilla, 48 to the operative field only, 23 to the axilla only and 6 others the details of which are unknown.

TABLE XX

POSTOPERATIVE IRRADIATION. EFFECT ON 5 YEAR SURVIVAL OF PATIENTS RECEIVING IRRADIATION AT CERTAIN TIMES AFTER OPERATION WAS PERFORMED (PORTMANN'S CLINICAL CLASSIFICATION)

Classification Group	No. of Cases	Immediate 1 to 6 weeks			Intermediate 6 weeks to 3 months			Delayed 3 months and over			Time Not Coded		
		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
I	142	69	36	52.1	39	16	41.0	31	14	45.1	3	0	0
II	90	36	7	19.1	28	7	19.4	26	10	38.4	0	0	0
III	24	6	1	16.6	11	2	18.1	6	2	33.3	1	0	0
IV	8	5	0	0	1	0	0	2	0	0	0	0	0
Unclassified	10	2	1	50.0	3	1	33.3	5	1	40.0	0	0	0
TOTALS	274*	118	45	38.1	82	26	31.7	70	27	38.5	4	0	0

* Same cases as referred to in Table XVII.

TABLE XXI

POSTOPERATIVE IRRADIATION. EFFECT ON 5 YEAR SURVIVAL OF PATIENTS RECEIVING IRRADIATION AT CERTAIN TIME AFTER OPERATION WAS PERFORMED (RICHARDS' STAGE OF DISEASE CLASSIFICATION)

Classification	No. of Cases	Immediate 1 to 6 weeks			Intermediate 6 weeks to 3 months			Delayed 3 months and over			Time Not Coded		
Stage		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival		Cases treated	5 yr. survival	
			No.	Per cent		No.	Per cent		No.	Per cent		No.	Per cent
I	29	18	13	72.2	4	3	75.0	5	3	60.0	2	0	0
II	59	26	12	46.1	21	6	28.5	12	9	75.0	0	0	0
III	94	41	14	34.1	25	10	4.0	28	7	25.0	0	0	0
IV	65	24	6	25.0	24	5	20.8	16	5	31.2	1	0	0
V	16	7	0	0	6	0	0	3	0	0	0	0	0
Unclassified	11	2	0	0	2	2	100.0	6	3	50.0	1	0	0
TOTALS	274*	118	45	38.1	82	26	31.7	70	27	38.5	4	0	0

* Same cases as referred to in Table XVIII.

uncertain as to whether one can draw any conclusions from data such as these.

Postoperative prophylactic irradiation may be defined as irradiation to areas other than to the operative field. The portals included the opposite chest, the homolateral axilla (in simple mastectomy cases), the supraclavicular region, the contralateral axilla, the anterior mediastinum and other areas. Some patients received therapy to more than one site, but the majority were to the opposite chest or to the mediastinum. The tumor dose for most sites was 1,500 r delivered in a long time interval. Twelve, or 41.3 per cent, of the 29 patients who had postoperative prophylactic irradiation survived five years (Tables XII, XIII and XIV). Twenty of these 29 patients were in Group I or II (Portmann).

COMMENT

From the statistics of this series, there is no clear evidence that preoperative or postoperative irradiation increased the five year survival rates, as compared to survival rates for operation alone. The patients having extension beyond the limits of regional lymph nodes may be considered to be incurable by operation or any biologically tolerated dosage of radiation. The question of radiation treatment in the patients who had local recurrences or metastases is to be the subject of a subsequent report. Suffice it to say, radiation treatment may be a locally palliative agent, even though it may not cure a general disease.

SUMMARY

1. In a series of 1,034 patients with carcinoma of the breast, who were seen at the Hospital of the University of Pennsylvania between 1923 and 1943, 1,029 cases were coded; of these, 110 received irradiation only, 557 had operations combined with irradiation, and 362 had operations only.

2. The cases were classified according to Portmann's Four-Group Clinical Classification, Richards' Five Stage of Disease Classification, and Richards' Clinical Index of Malignancy—for primary cases of carcinoma of the breast.

3. In this series, the gross five year survival statistics show that of the 1,029 coded cases, there was a five year survival rate of 49.7 per cent with operation only, 32.3 per cent with operation plus irradiation, and 5.4 per cent with irradiation alone. The over-all five year survival rate for 1,029 of the 1,034 patients was 35.5 per cent.

4. A statistical breakdown of the patients who had operation combined with irradiation indicated that of these 557 patients, there were 24 who had preoperative without postoperative irradiation, 34 who had preoperative and postoperative irradiation, 303 who had postoperative irradiation, 29 who had postoperative prophylac-

tic irradiation to sites other than the operative field, 157 who had irradiation for recurrences and metastases, and 10 who had unclassified irradiation. Some of these had prophylactic irradiation, castration, etc., in addition.

5. Of these 557 patients so treated as indicated above, the percentage of five year survival was respectively: 20.8 per cent, 29.4 per cent, 34.9 per cent, 41.3 per cent, 29.2 per cent, and 0.0 per cent.

6. The majority of patients receiving the various forms of preoperative or postoperative irradiation in this series had less than 3,000 tissue roentgens delivered over a relatively long period.

7. In this series the use of preoperative irradiation and the use of any form of postoperative irradiation did not show a higher five year survival rate over that obtained from operation alone.

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TRANSVAGINAL ROENTGEN THERAPY IN CANCER OF THE CERVICAL STUMP*

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CANCER in the retained cervix following supracervical hysterectomy falls into two categories, depending upon the lapsed time interval in which symptoms develop or the diagnosis is established. A two year time interval between the establishment of a positive diagnosis and the operation is quite generally accepted as a sufficient period to eliminate the probability of invasive cancer having been present at the time of surgery. This serves as an arbitrary period of time to classify cases into: (1) "true stump cancer" or (2) "coincidental cancer," a term used by Nuttall and Todd,[12] to designate those cases in which invasive cancer was probably present at the time the supracervical amputation was performed.

The average incidence of cancer of the cervical stump in 17,668 cases, reported by fourteen authors as taken from the literature, is 4.2 per cent. This figure assumes very little significance, however, because of the wide variation of the mean from the extreme. The combined statistics of Truelson[13] and Nielsen[11] represent an incidence of only 1 per cent in 4,219 cases of cervical cancer in Denmark. Ward and Sackett,[16] Black,[2] Hendricks[10] and Caulk, in 2,152 cases in the United States, on the other extreme, report an incidence of 7.7 per cent in their material.

The problem of "stump cancer" is probably most succinctly expressed by Hendricks and is well worth quoting: "Basically, cancer arising in the cervical stump at a date remote from hysterectomy, differs little in symptomatology, histological diagnosis or clinical behavior from cervical cancer occurring in the presence of the uterine fundus. Inasmuch as the chief factor setting these cases apart from the usual form of carcinoma of the cervix is a previous supracervical extirpation, it is probable that the incidence of carcinoma of the cervical stump varies directly with the number of times the supracervical operation is performed."

The literature on this subject of "stump cancer" is replete with discussion as to relative merits of surpacervical versus total hysterectomy. It is not the objective of this paper to delve into this controversy. However, the alarming incidence of so-called "coincidental cancer," as shown in Table 1, would indicate that the time and energy devoted to this endless discussion would have been far more profitable, as far as cancer is concerned, had it emphasized the importance of an accurate preoperative diagnosis rather than the type of operative procedure to be performed.

The survival rate by radiotherapy in

TABLE I

INCIDENCE OF COINCIDENTAL CANCER
(Various Authors)

	Number of Cases	
	Cancer in retained cervix	Coincidental cancer
von Graff[14] (1934)	581	137
Fricke and Bowing[7] (1940)	99	42
Carter[4] (1943)	11	6
Wall and Klingensmith[15] (1950)	62	27
Hendricks[10] (1951)	28	6
TOTAL	781	218 (27%)

* From the Radiological Clinics of Drs. Groover, Christie and Merritt. Presented at the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Mo., April 20–22, 1953.

"coincidental cancer" is exceedingly low. It is also well known that even a panhysterectomy, as routinely performed, is an inadequate method of curing invasive cervical cancer. It is indeed paradoxical that great time, expense and energy are devoted to the establishment of an accurate diagnosis in gastric cancer in which the prospect of cure is so poor in contrast to the hopefulness with which a hysterectomy is performed without eliminating the possibility of a highly curable form of cancer being present.

During the years 1932 through 1952, a total of 812 cases of cervical cancer applied for and received treatment in the Department of Radiation Therapy at Garfield Memorial Hospital. Fifty-five (6.7 per cent) of these cases are considered as true stump cancer.

These cases are from both private and clinic sources. By virtue of the organization and philosophy of the department, there was no controlled selection. Actually a community selection did exist with a high percentage of cases of clinic status representing the lower income and social levels. This is indicated by the fact that 38 per cent of the total group and 47 per cent of the stump group were of the Negro race.

The incidence of stump cancer by stages, as compared to the stage incidence of all cases treated during the same period, is shown in Table II.

The cases have been classified under the revised League of Nations classification. It has been a routine practice in this department to assign questionable cases into the prognostically more favorable stage in order not to raise unduly the rate for the earlier stages in this material.

All cases have been histopathologically proved, with only 3 adenocarcinomas in the entire group.

The difficulties in treating cancer of the cervical stump with radium are well recognized problems that have been discussed at length by Healy and Arneson,[9] Fricke and Bowing,[7] Cantril and Buschke.[3] The problem arises largely by virtue of the absence of an adequate cervical and uterine canal. The transvaginal roentgen therapy technique utilized in this series has been previously described by me.[5]

TABLE II

INCIDENCE OF CERVICAL STUMP CANCER BY STAGES AS COMPARED TO ALL CASES DURING THE SAME PERIOD

	Total Cases	Cervical Stump Cases
	812	55
Stage I	26%	37%
Stage II	43%	27%
Stage III	20%	20%
Stage IV	4%	3%
Modified	7%	11%

The survival rate in this series of cases is shown in Table III. While the total number of cases is too small to be of actual statistical significance, the fact that 16 five year survivals out of 25 total cases in which the transvaginal technique was used would indicate that this technique is an efficient method. Three of the transvaginal cases were adenocarcinomas of which one was a Stage I, who is alive and well thir-

TABLE III

SURVIVAL RATE, CERVICAL STUMP CANCER
1932 through 1947 42 cases

Indeterminate
Treatment not definitive 1
Untraced 0
Determinate

Stage	Ratio	Cases Survival, Per Cent
	Total Group	Transvaginal Group
I	17–13 (76%)	15–11 (73%)
II	13–6 (46%)	7–5 (70%)
III	8–0 (0%)	3–0 (0%)
IV	1–0 (0%)	0–0 (0%)
Modified	2–1 (50%)	0–0 (0%)
TOTAL	41–20 (48%)	25–16 (64%)

teen years after treatment; another Stage I, alive and well ten years after treatment, while the third case was clinical Stage III, who died twelve months after the beginning of treatment.

Table IV shows the five year survival rate of cervical stump cancer as reported by various authors in the literature. While the number of cases reported by each author is relatively small, the sum total of the more modern experience would indicate that the prognosis in cancer of the cervical stump is equally as good and probably even better than the average survival rate for all cases of cervical cancer. One might explain this on the basis that patients having had a surgical procedure, which interrupted the menstrual cycle, would report earlier for treatment when confronted with vaginal bleeding. Hahn,[8] however, in reporting on the Philadelphia plan for pelvic cancer control, found that the highest percentage of cases where a delay in the diagnosis of cancer was attributed solely to the physician, occurred in the cervical stump group. Also, the highest incidence of delay where the the physician played a contributory role, was again in the cervical stump.

An evaluation of the late radiation complications in the long-time survivals has been difficult to arrive at. I have personally made the follow-up examinations on the majority of the cases, but the follow-up on the remainder has been largely by correspondence. It is known, however, that 2 of the cured cases in the entire group developed a radiation stricture of the sigmoid, 1 with fistula. Two other cases developed obstruction to the small intestine, which at the time of surgery was found due to adhesions. The role of radiation therapy in producing the adhesions is not clear in these 2 cases. Varying degrees of vaginal atresia has occurred in the majority of the cases. Whether or not this can be regarded as a complication is problematical. It is rather difficult by any means to adequately treat cervical cancer and preserve a marital vagina.

The transvaginal specula and master cone arrangement, which I have described, was not used in any case before 1948. With this newer type of specula, the degree and incidence of vaginal atresia has been materially lessened. The problem of complications in the more recent material is now undergoing careful evaluation.

CONCLUSIONS

A small series of cases of cancer of the cervical stump, in which the transvaginal roentgen therapy approach has been used, is presented. The survival rate would indicate that this approach compares favorably with radium techniques from the standpoint of cure.

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Table IV

SURVIVAL RATE—CERVICAL STUMP CANCER—VARIOUS AUTHORS

Author	Year	Institution	Total Cases	Survival	Per Cent
Healy and Arneson[9]	1935	Memorial Hosp., N. Y.	36	5	14
Fricke and Bowing[7]	1940	Mayo Clinic	57	9	26
Donnelly and Bauld[6]	1949	Royal Vict. Hosp., Canada	20	3	6.5
Hendricks[10]	1949	Ohio State Univ. Hosp.	8	3	30
Ward[17]	1949	Woman's Hosp., N. Y.	49	21	42
Nielsen[11]	1952	Radium Center, Jutland	12	7	60
Baud[1]	1953	Curie Found., Paris	124	51	41
Caulk	1953	Garfield Mem., Wash., D. C.	41	20	48

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DISCUSSION

DR. FRANK R. SMITH, New York, New York. It is a great privilege to discuss Dr. Caulk's presentation. As he stated, Dr. Caulk has presented the technique of this method of approach in a previous publication. I was delighted that he took up the question of prophylaxis against cancer of the cervical stump. The old question in the gynecological clinics of whether to do a total or subtotal hysterectomy is now fairly dead, I think. The old adage that the mortality of total hysterectomy was much greater than that of subtotal hysterectomy, was much greater than the incidence of carcinoma of the stump, is certainly not true today.

The point that Dr. Caulk brought out is certainly well taken—that the cervix should be investigated before any type of surgery is done. If cancer is present, I doubt if simple total hysterectomy is an adequate procedure.

The incidence has been referred to, and while Dr. Caulk gives it as being about 4 per cent, it has tremendous variation, and most of the instances are considered as instances of cervical stump in that individual clinic, in proportion to their total cancers of the cervix. There is very little accurate knowledge of how large the incidence of cancer to cervical stump is to subtotal or incomplete operations.

Dr. Martzloff reported—after a rather complete review of the literature—that this incidence was about 1 per cent. I have no information to dispute that or confirm it.

The results of carcinoma of the cervical stump had been notoriously poor, according to the reported statistics, until recent years. The results in the report of Healy and Arneson in 1935, to which Dr. Caulk refers in Table IV, were notoriously poor; they were much poorer than the results that have later come to be the more popular conception of the way cancer of the cervical stump responds. I think most clinics today will agree that cancer of the stump is as favorable to treatment as cancer when the uterus is present.

As to diagnosis, the reference to Hahn's report—the so-called "Philadelphia plan"—is interesting, because of the higher incidence of doctor delay in bringing cancer of the cervical stump to treatment, as opposed to the proportion of blame that could be placed on the physician in cancer of the cervix when the uterus was present. I think that shows that in spite of our publicity programs, our educational programs for doctors, the doctors as well as the patients are lulled into a sense of false security by the fact that the patient has had an operation.

As to the treatment, Dr. Caulk has presented one method of treatment. There have been many advances in the treatment of cancer of the cervix, in general. I think they generally fall into the classes of irradiation and surgery. The cervical stump lends itself, anatomically, to radiation therapy. It is especially adapted to interstitial irradiation. The advances in irradiation have been largely in the field of precision irradiation, first, and second, in the increase of tumor dosage delivered. With the accomplishment of an increase in tumor dosage, there has been a resulting increase in the damage to surrounding and adjacent normal tissues.

In 1934, at Memorial Hospital in New York, I was able to show that our stump cancer group had an incidence of fistulas following treatment which was more than three times that of the cervical cancer treated when the uterus was present. We found that where interstitial irradiation was used, it was twice what the incidence of fistulas was in untreated cancer. This untreated cancer, in turn, was twice as high as the incidence of fistulas in normal carcinoma of the cervix when the uterus is present.

It is interesting that the curve of fistula incidence during the years practically parallels the prevalence of interstitial irradiation usage for each year.

Dr. Caulk's method is a definite advance. I have used it. I am pleased with it. I think it is a great advance, with his translucent cone, which gives practically double the field of exposure of the old fashioned metal cone which we used at Memorial. I think he is to be commended for this usage.

I think he still has a large enough number of cases to evaluate the optimum dosage and the damage which will result.

The surgical advance has been largely due to supportive treatment, and we have been able to carry on surgery which formerly was not possible. At Memorial Hospital, since 1947, we have treated all cases of carcinoma of the cervix with radical surgery, and have achieved an over-all rate of 47.7 per cent. Unfortunately, our incidence of stump cancers is still 8.1 per cent of all cancers.

I would suggest that there is no one treatment for cancer of the cervical stump, but the ideal may be to use a combination of accurate irradiation combined with skillful surgery. Both should be used more radically, using both as lethal weapons to treat a lethal disease. They should be used in supporting fashion rather than as antagonistic methods. Possibly we should use some systematic methods such as Ruth Graham has referred to, in deciding which cases are suitable for which type of treatment.

The difference in the approach and methods of collecting statistics has proved that the only valuable fact is the over-all five year cure rate, taken in unselected cases.

I was glad that Dr. Caulk did not go into the question of this much abused precancerous lesion called by the misnomer of "cancer in situ," unless he included it in these modified cases and charts.

I enjoyed reading Dr. Caulk's paper and hearing his excellent presentation, and I want to congratulate him on the results which he has presented here.

RADIATION SICKNESS

A STUDY OF ITS RELATION TO ADRENAL CORTICAL FUNCTION AND THE ABSOLUTE EOSINOPHIL COUNT*†

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IN RECENT years, increasing attention has been paid to the study of a possible relationship between adrenal cortical function and radiation morbidity and mortality. Most investigations have been concerned with the latter factor and evidence submitted thus far has been somewhat contradictory. Studies directed toward radiation morbidity or "radiation sickness" have been largely based on inferential evidences carried over from animals to man, or on the effects of endocrine replacement therapy in man.

The present study offers what we believe to be the first controlled series of observations on changes in adrenal cortical status in man undergoing deep roentgen therapy. It began in July, 1951, when one of us (K.W.S.) suggested that a study be undertaken to determine the cause of the peripheral eosinophilia encountered in many of our patients undergoing external irradiation for carcinoma of the uterine cervix.

METHODS

Forty cases were used in the initial study. Thirty-six of these were undergoing deep roentgen therapy for squamous cell carcinoma of the cervix and 2 for adenocarcinoma of the cervix. One case was receiving therapy for squamous cell carcinoma of the vagina and 1 for serous cystadenoma of the ovary.

In all cases, therapy was limited to one area of the body, the pelvis. In all cases, the quality of radiation employed was the same (400 kv. [peak], 5 ma., Thoraeus filter, 0.44 mm. Sn plus 0.25 mm. Cu; half-value layer 3.9 mm. Cu). Treatment was given daily in all cases, with the exception of Sunday. Patients were given either 3,000 or 3,500 roentgens total dose to the center of the pelvis over an average period of about twenty-eight days. The average daily dose was 300 to 350 r in air.

An attempt was made to determine the basal absolute eosinophil count and to perform a modified Thorn eosinophil response test[29] at weekly intervals. This was not always successful because of extraneous circumstances, and some patients had only two or three determinations in the course of their treatment.

The basal absolute eosinophil count was determined on fasting venous blood obtained as near 8:00 A.M. as possible to obviate the error that might arise from the physiological, diurnal variations noted by Rud[23] and by Halberg and Visscher.[7] Blood samples were kept in double oxalate tubes until the counting process took place several hours later.

The actual counting process was carried out according to the method of Randolph,[21] utilizing a mixture of phloxine in propyleneglycol, and methylene blue as diluting fluid. Retested Exax pipettes and a Levy counting chamber with Fuchs Rosenthal ruling were employed in all counts. All counts were done in duplicate so that four chambers were counted. An accuracy of ± 2.5 per cent is said to be attainable by this method for counts in the normal range.[31] One individual carried out the majority of the counts.

The modified Thorn eosinophil response test was carried out at the same time as the basal total eosinophil count by injecting 20

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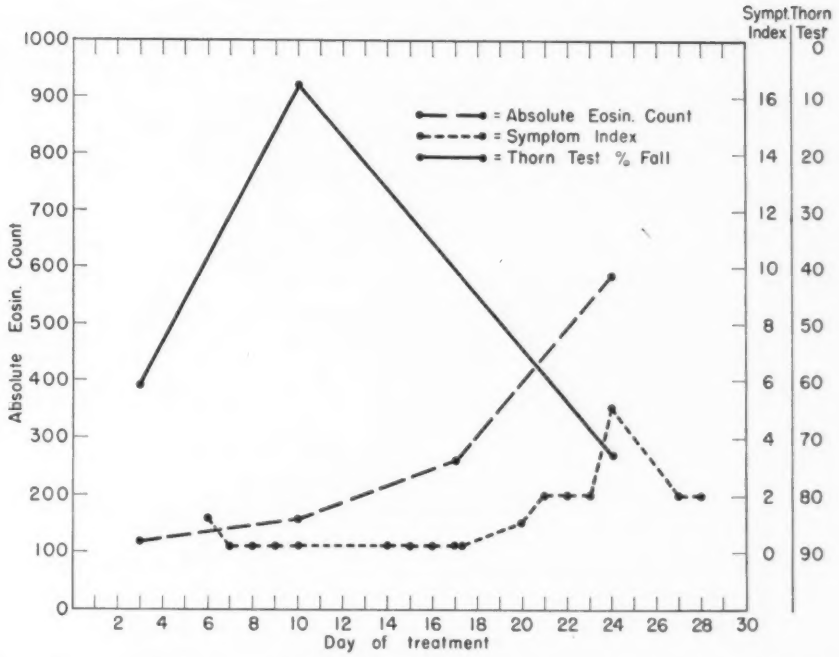

Fig. 1. Case 29. The variations of the absolute eosinophil count, the arbitrary symptom index, and the four hour response of circulating eosinophils to ACTH during the course of treatment are graphically depicted. Each point represents a single determination.

mg. of ACTHAR (Armour brand of ACTH) intramuscularly immediately after securing the blood sample for the initial count. A second venous blood sample for determination of absolute eosinophils was then obtained in four hours. Thorn used 25 mg. of ACTH in the original description of his test, but in a later report he showed that there would be no significant difference in eosinophil response when 20 mg. of ACTH was used instead of 25 mg.[20] Twenty milligrams were used in our tests in order to best utilize the 40 mg. vial available to us.

According to Thorn and his co-workers, an absolute decrease in circulating eosinophils of 50 per cent or more, four hours after the ACTH injection, indicates a satisfactory adrenal cortical response. A fall of less than 50 per cent is taken to indicate some impairment of adrenal reserve.

In a limited number of cases, urinary excretion of corticosteroid-like substances was determined according to the method of Talbot, Saltzman, Wixom and Wolfe.[28] This procedure depends upon the extraction of corticosteroids from urine (by aqueous extraction from benzene under the conditions of the procedure) and the colorimetric determination of the extracted corticosteroids following the reduction of suitable copper reagents.

In addition to the basal total eosinophil count and the determinations of adrenal cortical function mentioned above, the last 20 patients in the group under study were subjected to daily questioning regarding possible symptoms of radiation sickness. Nausea, vomiting, anorexia, headache, vertigo, excessive thirst, weakness and colic were considered to be suggestive of radiation sickness and each of these symptoms was carefully inquired into each day by the same interrogator. When present, each of the symptoms listed above was rated from 1 plus to 3 plus, depending upon their severity in the judgment of the interrogator. The sum of the plus values for any particular individual on any one day of the treatment schedule was taken as the index of severity of radiation sickness for that

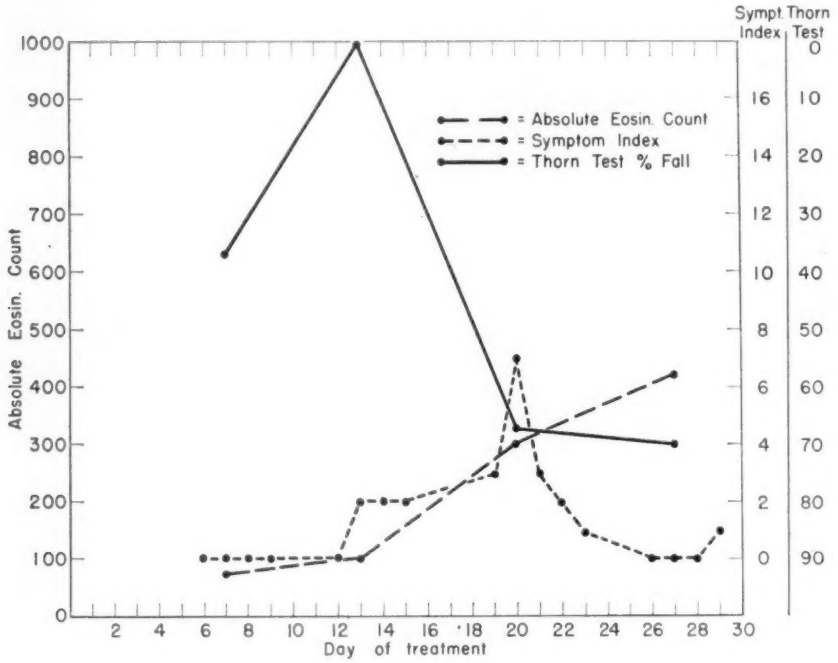

FIG. 2. Case 49. See legend for Figure 1.

patient, for that particular day.

Utilizing the above data, a number of different curves were assembled.

1. The variations, in the course of treatment, of the absolute eosinophil count, the ACTH-eosinophil response test, and (in the last 20 patients) the symptoms of radiation sickness were plotted for each patient. The ordinates were, respectively, the absolute total eosinophil count, the percentage fall of eosinophils following ACTH injection, and an arbitrary scale used to designate the severity of radiation sickness each day as noted above. The abscissa for each curve was the treatment day (0–35). Good examples of these curves are the graphs of Cases 29, 49, 26 and 33 (Fig. 1–4).

2. A composite chart was made by taking the average values for all the patients in this study. The treatment periods were divided into five day intervals, and the mean values of all the basal eosinophil counts, of all the percentage drops of eosinophils after ACTH, and of all the radiation sickness indexes, were computed for each of these five day intervals (Chart 1). The points thus determined were plotted on a single graph with individual ordinates for each of the three groups cited above. Lines were drawn connecting the respective mean values for successive five day intervals of each group and a convenient reference was thus established to compare the relative changes of adrenal reserve, absolute basal eosinophils, and radiation sickness with one another throughout the successive intervals of therapy (Fig. 5). The basal eosinophil curves, and the Thorn test curves were derived from data on 40 patients. The radiation sickness index curve was taken from the last 20 of these patients only, no record having been kept of the symptoms in the first 20 cases of the study. The over-all similarity of the radiation therapy given each of the patients in this study enables the reviewer to consider the group as an integral unit in evaluating the results obtained.

3. Curves similar to those constructed for Figure 5 were determined by subdividing the patients into two groups: (a) those falling into the premenopausal group plus those having had their last menstrual period less than six months prior to the onset of therapy, and (b) those having had their last menstrual period more than six months prior to the onset of therapy. This was done in an attempt to determine the possible effects of the (relative) presence or absence of the female sex hormone upon the factors under study (Fig. 6 and 7, Charts II and III).

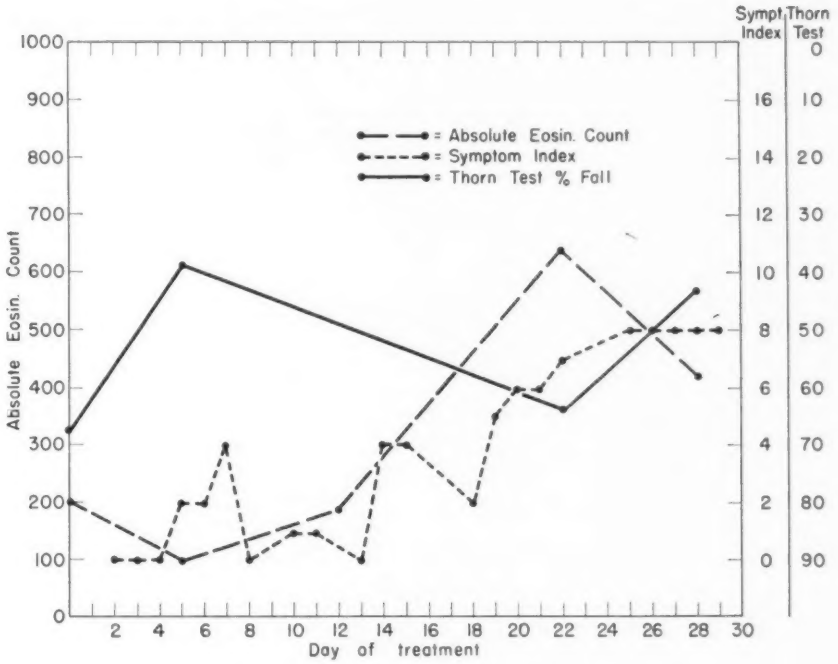

FIG. 3. Case 26. See legend for Figure 1.

All of the above determinations were repeated using a volume dose estimation, rather than a period of time, as abscissa for the graphs. Briefly, this consisted of estimating the percentage of total tumor dose administered for any "round" of therapy or fraction thereof. Each pelvic field was then assigned a certain percentage value for each round, the percentage having been estimated by a consideration of the relative amount of tissue irradiated in each field in an average patient. Thus, for the conventional five fields of the pelvis, the anterior field was assigned 28 per cent, the right and left posterior obliques 20 per cent each, and the right and left laterals 16 per cent each. An estimated volume dose could thus be established for any particular time period of the treatment in arbitrary units.

A consideration of the results obtained graphically using the arbitrary volume dose units rather than the actual time units, however, showed no significant difference for any of the determinations, and so the more readily acceptable time unit has been maintained in the charts.

RESULTS

A study of the individual patient's charts, where sufficient determinations were carried out to enable workable curves to be constructed, permits certain comparisons to be made of the eosinophil count, adrenal reserve as determined by the modified Thorn test, and radiation sickness index as defined in the previous section. Reference to Figure 1 shows that for this patient (carcinoma of the cervix LNS III) the initial value for the modified Thorn test, obtained on the third day of treatment was 61 per cent (fall in eosinophils four hours after ACTH). This falls within the normal range at this time. The basal absolute eosinophil count at this time was 122 cells per cubic millimeter and also falls within the limits of normal (normal 60 to 200 per cu. mm.).[9] No index of symptomatology was recorded at this time. On the tenth day, the patient is asymptomatic. The modified Thorn test carried out at this time shows only an 8 per cent fall, and compares to levels found in Addisonian patients by Thorn and others. The basal

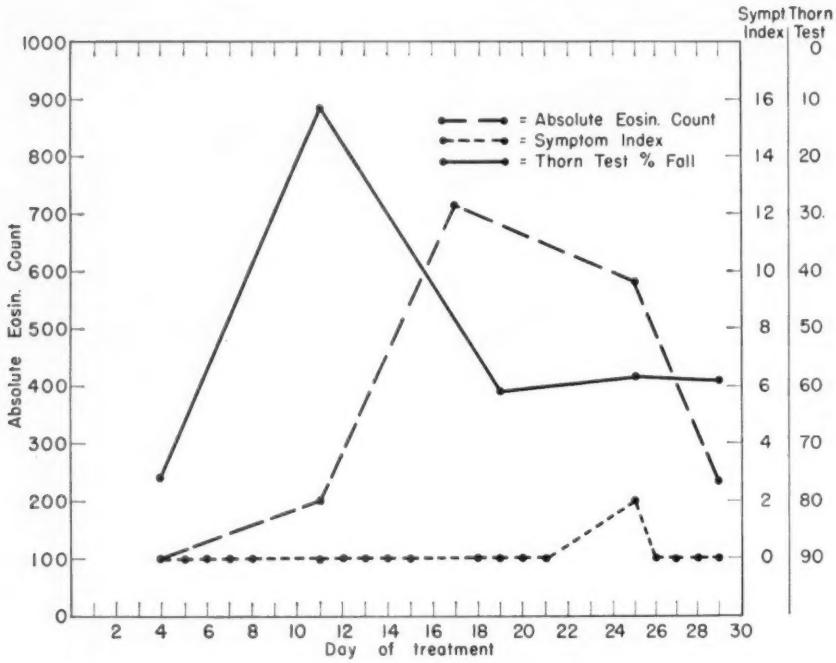

FIG. 4. Case 33. See legend for Figure 1.

absolute eosinophil count has shown a slight rise from its initial level. On the seventeenth day, the patient remains asymptomatic, while the absolute eosinophils have shown a slightly greater increase, numbering 266 per cu. mm. No Thorn test was carried out on this date. On the twenty-fourth day, the Thorn test has returned to a normal level (73 per cent drop) while the absolute eosinophils have increased above normal to a level of 584 per cu. mm. At the same time, the patient has shown a gradual increase in severity of radiation sickness symptoms beginning on the seventeenth day, and the arbitrary index of 5 has been reached on the twenty-fourth day.

In this patient, the lowest recorded level of adrenal cortical function occurred on the tenth day of treatment, when the patient was asymptomatic. As the level of adrenal cortical function returned to normal, there was a rise in the total eosinophils followed by a rise in symptomatology. The maximum symptomatology occurred at the time of the maximum recorded eosinophil count, and at the time of the most adequate adrenal cortical function as judged by the modified Thorn test.

The same basic relationships were noted in Case 49 (Fig. 2). Symptoms were at a minimum at the time of maximum lack of adrenal reserve, and increased to a maximum, with the absolute eosinophil count as adrenal cortical function returned to the normal range and beyond. Urinary excretion of corticoid substances was determined for this patient. On the fifteenth day of treatment, it amounted to 0.218 mg. in twenty-four hours, while on the twenty-ninth day of treatment excretion of corticoid substances had risen to 0.301 mg. in twenty-four hours, thus adding weight to the improved adrenal cortical function denoted by the modified Thorn test.

The curves of Case 26 (Fig. 3) indicate that the basic relationships discussed above hold true here as well, with the exception that the modified Thorn test shows two peaks, neither one of which is far below the accepted normal.

Case 33 (Fig. 4) shows another variation of the basic relationship. In this instance

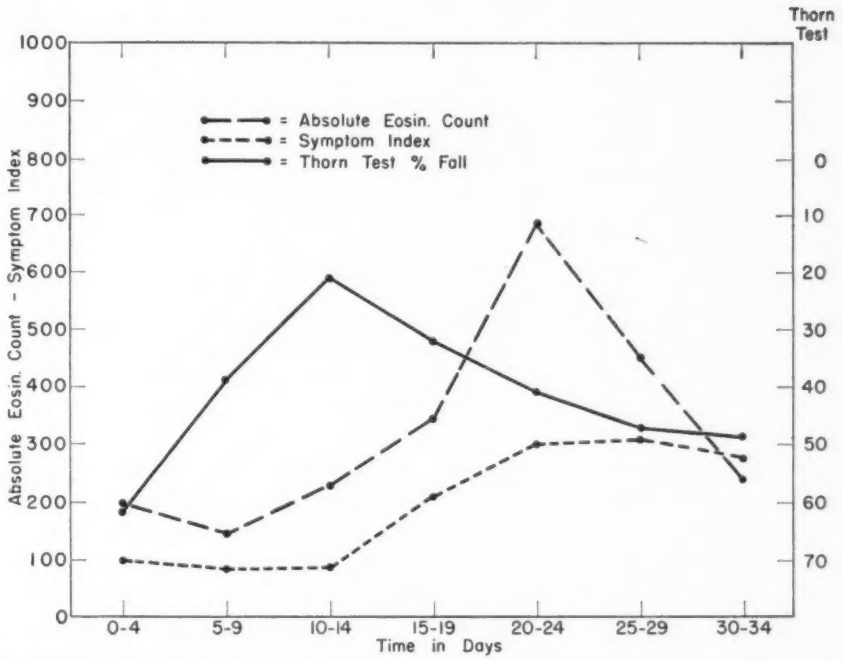

Fig. 5. (Chart 1) Total group. The total treatment period has been divided up into arbitrary five day intervals. Each point represents the mean value for all the determinations in that interval.

the absolute eosinophil curve and the modified Thorn test curve show the same basic relationship to one another, but there is little or no evidence of radiation sickness in this patient as noted by the nearly flat symptom index curve. A rise in the absolute eosinophil curve without a similar rise in the symptom index curve was noted in 5 out of 20 cases. On the other hand, a rise in the symptom index curve without some rise in the eosinophil curve could be made out in only 2 of the 20 cases, and in 1 of these, the initial point of the eosinophil curve was abnormally elevated initially.

Corticoid excretion studies were felt to be of no significance if only one determination was carried out on a patient. Two determinations at different time intervals in the course of therapy were available on only 2 patients other than the one previously quoted. In both instances, the corticoid excretion was lower at the time of relative decrease in adrenal cortical reserve as denoted by the modified Thorn test, and higher with more adequate adrenal cortical status as denoted by the same test. The two tests were thus in agreement in these instances.

A study of Figure 5 bears out, for the group as a whole, the trends alluded to in the study of the curves of individual patients. It should be remembered that the data set down in Chart 1 and recorded graphically in Figure 5 represents a composite value. The number of determinations that entered into the compilation of the mean value for each of the factors under study at successive five day intervals of the therapy period can be read from Chart 1. Although the radiation sickness index could be obtained from only the last 20 patients of the 40 included in this study, it should be noted that the number of determinations at each five day interval for this group is higher than for either of the other two factors under study in the same interval. This is due to the fact that an index was computed daily or almost daily for each patient, while the basal absolute eosinophil test and the ACTH-eosinophil response were carried out only once a week in the average patient.

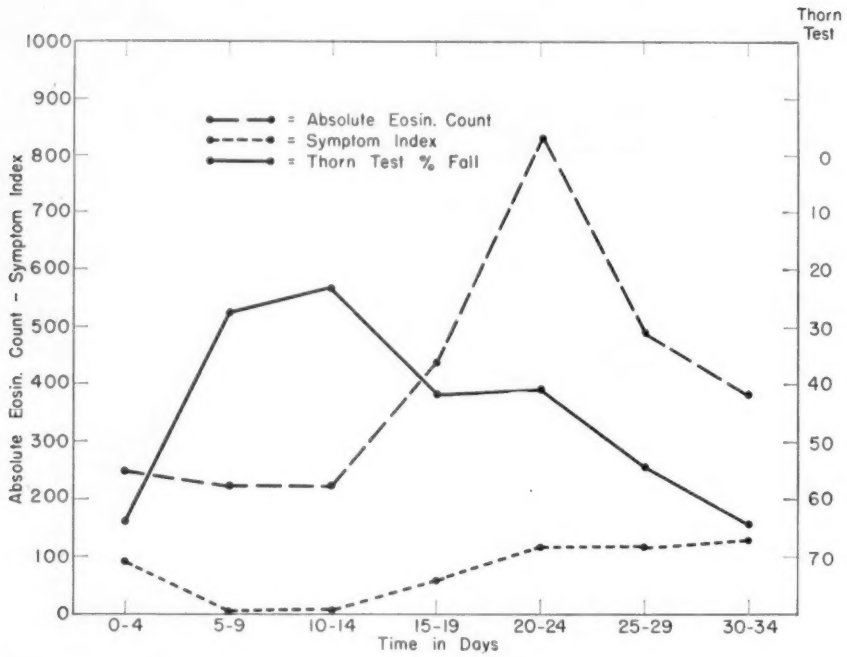

FIG. 6. (Chart 11) Cases falling into premenopausal or less than six months postmenopausal category. The graphing is similar to Figure 5.

As may be seen in Figure 3, the initial value of the ACTH-eosinophil four hour response test was 62 per cent, a value which, according to Thorn and his associates, denotes normal adrenal cortical function. By ten to fourteen days, however, this value had fallen considerably below normal to 21 per cent. A gradual increase toward normal is then seen in the face of continued treatment until a border line normal value of 51 per cent has been established in the thirty to thirty-four day interval. (Since relatively few patients were treated beyond thirty days, the number of determinations for all factors in the 30–34 day group is small.)

The symptom index curve shows relatively little in the way of symptomatology until after the ten to fourteen day period when a gradual rise is noted until the twenty to twenty-four day interval is reached. Here the curve flattens out and a very slight return toward the base line is noted at the thirty to thirty-four day period.

The curve of the basal absolute eosinophils resembles the symptom curve in a number of respects. It starts out at the zero to four day period within the normal range and by five to nine days has shown a slight initial drop. By ten to fourteen days, it has shown a slight rise above the base line. From this point on, the rise is more abrupt until a peak of 687 cells per cu. mm. is reached at the twenty to twenty-four day period (the highest individual count was 2,472 cells per cu. mm.). Just as the symptom index curve leveled off after this interval, the eosinophil curve shows a fall toward normal values in the remaining two intervals.

The statistical significance of the peak values of each curve in relation to its initial basé line value has been determined and in each instance has been found to be significant. These determinations are summarized in the appendix.

Attention should be called to the fact that for the group as a whole, little or no symptomatology was evident at the time when maximum adrenal cortical exhaustion was present as indicated by the modified

Days	0-4	5-9	10-14	15-19	20-24	25-29	30-34	
Absolute Eosinophil Count	24	19	18	21	19	20	8	Number of determinations
	197	*151*	*227*	*344*	*687*	*458*	*234*	*Average cells / cu.mm*
Thorn Test	21	20	19	19	18	19	7	Number of determinations
	62	*39*	*21*	*32*	*41*	*46*	*51*	*Average % fall*
Symptoms	41	63	44	66	65	62	12	Number of determinations
	95	*83*	*89*	*206*	*300*	*306*	*275*	*Symptom index*

Chart I. Number of determinations entering into compilation of mean values for the eosinophil count, Thorn test and symptom index in each five day period for the group as a whole. The data for the eosinophil count and Thorn tests were computed from 40 patients. The data for the symptom index were drawn from the last 20 of these (Fig. 5).

Thorn test. The increase in symptomatology appeared to parallel in time the increase in basal absolute eosinophils, and when the eosinophils began to decline, the symptom index curve leveled off. This parallelism suggests that both curves reflect variations in some other (unknown) factor or, less likely, are etiologically related to one another.

When the cases in this study are divided into two groups, one premenopausal and six months beyond (to allow for sustained estrogen levels) and the other six months beyond menopause, evaluation is on less firm ground because of the relatively small number of cases in the former group (Charts II and III; Fig. 6 and 7). As can be seen, the basic relations of the three curves, as noted before, can again be made out. There does appear, however, to be a marked increase in symptomatology in the second group who supposedly have lower estrogen levels and, for the symptom index, the number of determinations may be sufficient to be of significance. Furthermore, studies in progress at the present time on a group of patients receiving therapy for radiation sickness, strongly support the

Days	0-4	5-9	10-14	15-19	20-24	25-29	30-34	
Absolute Eosinophil Count	8	5	6	7	3	8	2	Number of determinations
	246	*224*	*226*	*437*	*832*	*493*	*386*	*Average cells / cu mm*
Thorn Test	8	5	7	7	3	8	2	Number of determinations
	64	*28*	*23*	*42*	*41*	*54*	*64*	*Average % fall*
Symptoms	13	17	12	22	18	18	3	Number of determinations
	92	*6*	*8*	*59*	*122*	*122*	*133*	*Symptom index*

Chart II. Data derived from those patients falling into premenopausal, or less than six months postmenopausal, category (Fig. 6).

Days	0-4	5-9	10-14	15-19	20-24	25-29	30-34	
Absolute Eosinophil Count	14	13	12	13	16	11	6	Number of determinations
	177	*128*	*200*	*281*	*660*	*457*	*183*	*Average cells / cu.mm*
Thorn Test	12	12	11	11	15	11	5	Number of determinations
	59	*51*	*16*	*24*	*41*	*40*	*46*	*Average % fall*
Symptoms	26	44	34	44	47	43	9	Number of determinations
	104	*116*	*109*	*280*	*368*	*379*	*322*	*Symptom index*

Chart III. Data derived from those patients of study who were at least six months beyond menopause (Fig. 7).

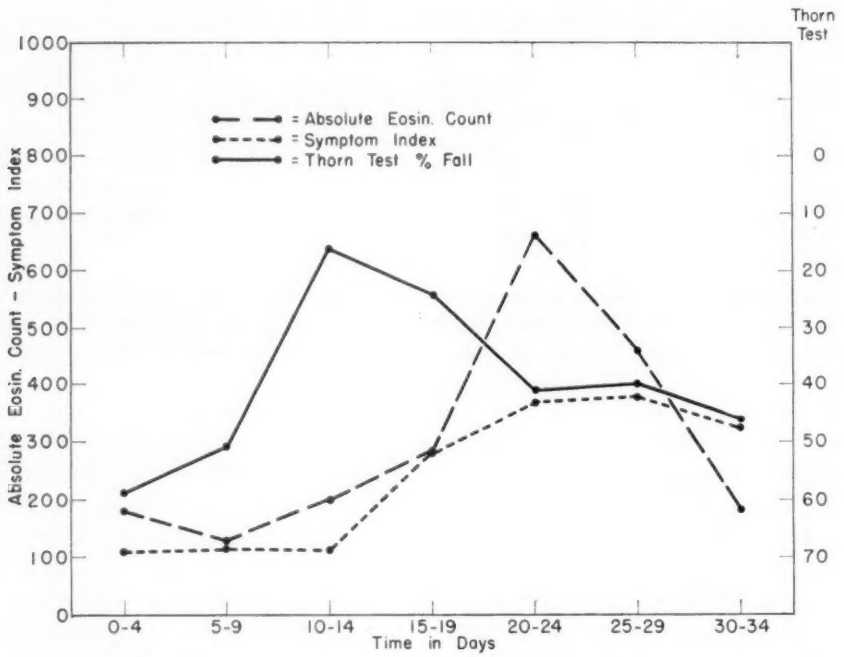

FIG. 7. (Chart III) Cases falling into group at least six months postmenopausal. Graphing similar to Figure 5.

differences in symptomatology noted in the above two groups.

COMMENT

Numerous clinical studies of radiation sickness have been carried out and reported in the literature. In recent years, reports by Lofstrom and Nurnberger,[13] by Taber,[27] and by Porter,[19] all include bibliographies containing many references to studies of radiation sickness. The host of substances recommended at various times for the therapy of radiation sickness bears testimony to the paucity of substantiated knowledge relating to fundamental causes of this phenomenon.

The human being as an experimental animal leaves much to be desired in most instances. Yet, from another standpoint, he is the ideal subject in a clinical study since he eliminates the hypothetical carry-over from one complex biological system to another. It occurs to us that the greatest criticism that can be leveled at previous clinical studies of radiation sickness is their universal failure to eliminate, or attempt to eliminate, the overwhelming number of variables that are introduced by lumping together in one study patients receiving various amounts of radiation, directed to various parts of the body, over various periods of time.

If one attempts to limit as many of these variables as possible, he is in a considerably better position to subordinate the occasional erratic biological response that must be expected within the larger body of accumulated data.

We have attempted to do this, as far as possible, in the present study. The results that we have obtained thus far, may merit comparison to related studies carried out in the past.

A. *The Adrenal Cortex and Radiation.* In 1942, Leblond and Segal,[12] working with rats, showed that in the intact animal, roentgen irradiation over the lower abdomen produced involutional changes in the thymus, spleen and distant lymph nodes, These changes were not found in adrenalectomized animals receiving the same type of irradiation. In their intact animals, the adrenals showed a significant increase in weight after intense irradiation of the lower abdomen. Histopathologically, the

hypertrophy was confined to the cortex where the fascicular zone showed thickening, with decrease of lipid globules. These investigators believed that release of histamine or similar substances in irradiated tissues was responsible for the effect upon the adrenal and other organs.

Four years later, Dougherty and White[1] pointed out the similarity between the described changes produced in lymphoid tissue by roentgen irradiation and those following a single injection of either pituitary adrenotrophic hormone or adrenal cortical preparations. From their own experimental work with total body irradiation in mice, they found that small doses (10 r) of roentgen rays produced unmistakable alterations in lymphoid tissue structure and function only in the presence of an intact pituitary-adrenal cortical mechanism, but that large doses (200 r) produced these changes even in the absence of adrenals. They also noted a decrease in the sudanophilic material of the adrenal several hours after 200 r whole body irradiation.

In 1947, Patt, Swift, Tyree and John[16] showed that rats given 650 r total body irradiation showed a 40–50 per cent decrease in the cholesterol content of their adrenals in three to six hours and that in two days, the cholesterol content began to rise, reaching a level some 100 per cent above normal at seven days. This was followed by a return toward normal at nine to eleven days and a further increase at fifteen days. In 1948, Patt, Swift, Tyree and Straube[17] showed that hypophysectomy performed one week prior to irradiation prevented the adrenal changes noted above.

Ellinger,[2] in the same year, expressed the concept that radiation sickness represents a typical case of the "adaptation syndrome" of Selye, the unspecific response of the body to stress, irrespective of its causation by chemicals, bacterial toxins, or physical agents.[24] Following a suggestion by Weichert[30] in Germany, Ellinger investigated the use of desoxycorticosterone acetate in radiation intoxication. He found that mice protected by a daily dose of 0.5 mg. DCA showed almost a 50 per cent reduction in mortality after the administration of LD_{50} of total body irradiation. In the next year, Ellinger, with Roswit and Glasser,[3] carried out a clinical study on 50 patients whose radiation sickness was treated with DCA. Of these, only 3 failed to show some response to the therapy.

Patt and his co-workers,[26] in 1949, were unable to duplicate Ellinger's reduction in mortality of mice to LD_{50} total body irradiation when protected by daily injections of DCA. These investigators, in fact, found the same survival rate in (1) intact mice, (2) mice given 0.5 mg. DCA daily for two weeks after irradiation, (3) mice given whole adrenal cortical extract 0.2 cc. twice daily for two weeks following irradiation and (4) adrenalectomized mice given 0.2 cc. adrenal cortical extract and salted drinking water.

In 1950, Smith, Smith and Thompson[25] found that intraperitoneal injections of cortisone or subcutaneous injections of ACTH failed to increase survival time or number in mice subjected to total body irradiation in the LD_{50} range.

In 1951, Kohn[10] showed that a transient increase in serum chloride and cholesterol in rats exposed to a dose of total body irradiation just below the LD_{50} per cent could be prevented by daily administration of desoxycorticosterone or lipoadrenal extract.

In a clinical and experimental study reported in 1951, Taber[27] reported that 12 of 14 patients were relieved promptly of radiation sickness by several injections of 10 mg. doses of ACTH. In a limited animal study, he felt that he had demonstrated that ACTH administered daily in doses of 0.15 mg. per kilogram of body weight had saved the lives of mice exposed to 300 r total body irradiation. The extremely small number of animals used in these experiments, however, render the results inconclusive.

Finally, in 1952, Porter[19] reported on 36 patients undergoing roentgen therapy who were studied by frequent eosinophil counts. Ten of these patients developed radiation sickness in which a fall in eosinophil count followed within several hours, usually not exceeding twenty-four. Symptoms in these patients cleared with the dropping of the eosinophil count even though treatment was continued. Porter interprets this as evidence of an adrenal response alleviating radiation sickness.

The only deduction which seems indicated from the mass of evidence cited above is that either local or total body irradiation is capable of causing a cyclic variation in the output of adrenal cortical steroids. The precise effect of these variations on radiation morbidity and mortality in animals and man is not clear-cut.

From the evidence, one would be tempted to explain the beneficial effects of DCA therapy in Ellinger's series on some specific pharmacological action of the hormone other than simple replacement of a deficiency in the adrenal cortical output. Rose,[22] for example, has shown that DCA increases the deactivation of histamine in adrenalectomized rats. It is interesting to note also that Ellinger[4] in 1952 showed that cortisone increased the mortality of mice to doses of radiation above the sublethal level. Likewise, in Porter's series, the fact that the sickness preceded the drop in eosinophils suggests that these patients had adequate adrenal cortical reserve at the time of the onset of their sickness, the acute episode of nausea or vomiting acting as a nonspecific stress upon the adrenal.

Our own study indicates that continued irradiation under the circumstances previously described, causes a gradual depletion of adrenal cortical reserve followed by recovery. From the evidence cited earlier in this report, there was no suggestion that this depletion of adrenal cortical function was related to radiation sickness. Likewise, injections of ACTH in 20 mg. doses (used for the modified Thorn test) failed to show any evidence of relieving radiation sickness, when present.

B. *Eosinophils and Radiation.* Minot and Spurling[14] in 1924, commenting on the effect of short wavelength roentgen therapy state that the work in the literature at that time indicates that an initial fall in eosinophils, followed by an increase over a period of days to weeks, and then a return to normal, may be expected in patients undergoing roentgen therapy. From their own experience, they state that eosinophilia following irradiation appears to occur particularly as a result of repeated exposures.

Earlier Pfahler,[18] studying the blood changes in radiologists by the questionnaire method, had reported a marked increase in eosinophils in a few cases.

In 1936, Goodfellow[5] noted that the circulating eosinophils are often greatly increased by therapeutic exposure to gamma rays. He quotes a number of studies on humans and animals exposed to various types of radiation where a late eosinophilia was noted.

Kornblum, Boerner and Henderson,[11] on the other hand, reporting in 1938 on the effects of clinical therapeutic irradiation on the normal blood cells, state that the effect on the monocytes and eosinophils is apparently to cause a slight decrease in number.

In 1951, Moses and Platt[15] reported on 3 workers who received an indeterminate dose of radiation while sanding the copper dees of a cyclotron. Two of these showed a high eosinophil count immediately after exposure. On the basis of these findings, these authors suggest that the total circulating eosinophil count may be a useful index of exposure to radiation.

Hempelmann, Lisco and Hoffman,[8] in 1952, wrote a detailed report of 9 patients involved in accidental nuclear reactions at the Los Alamos Laboratory. Two of these cases showed a definite eosinophilia while 3 more showed slight elevations. They note that many Japanese survivors of the atomic bomb explosion showed a relative increase in the percentage of eosinophils, particularly in the period from eight to twelve weeks after exposure. The percentage of eosinophils was roughly proportional to the radiation dose in the survivors. These authors note also, from their own study, that a fall in eosinophil count occurred only in those patients with overt signs of injury. The eosinophil count of those patients who experienced no illness either remained unchanged or was increased.

Our own findings, as noted previously, confirm the development of an eosinophilia after repeated irradiation. The exact relation of the eosinophilia to the changes in the adrenal cortex remains an unanswered question. It is known that total bilateral adrenalectomy in dogs produces an immediate rise in eosinophils with a gradual stabilization over a period of weeks at five to ten times the control level. Patients with chronic adrenal insufficiency (Addison's disease) may show little or no elevation of circulating eosinophils by direct count.[20]

In our own study, the eosinophils began to rise, on an average, five to ten days before evidence of maximal adrenal cortical insufficiency had been shown. The continued rise, in spite of the return of adrenal status to normal, speaks against a pure adrenal cortical control of the eosinophils in these cases.

The correlation between the eosinophil curves and the symptom curves in our patients suggest that both may be a response to some common etiological factor. The possibility that both the elevation of eosinophils and the in-

crease in symptomatology may be related to increased levels of circulating blood histamine, such as has been postulated by Ellinger and others, is an attractive hypothesis, and a study of histamine levels in these patients is being commenced at the present time.

The similarity of the two curves provides an opportunity, also, to study the effects of various drugs on radiation sickness, utilizing the eosinophil curve as an objective criterion for effectiveness of the drugs tested. This study is at present in progress, and will be reported on at a later date.

One word of caution must be put forth. Desultory absolute eosinophil counts done on patients receiving treatment to the thorax and to the head have been carried out by us, and the results suggest that the eosinophil count in these patients may show no change or may even fall. No attempt has been made in these instances to determine the adrenal status, presence or absence of symptoms, etc., and they are not included in our analysis. It must be emphasized that we only present evidence to support the described changes in eosinophils, adrenal status, and symptomatology under the conditions in which we carried out this study.

Finally, the increase in symptomatology in the postmenopausal group deserves some mention. The work of Graham and Graham[6] on the modification of resistance to ionizing radiation by humoral agents indicates that female Swiss mice show a diminished vulnerability to 400 r total body irradiation when given estrodial benzoate or estrone before exposure. Stilbesterol had a quite different effect from the natural estrogens, being comparatively inert in protective action in females before or after irradiation. These authors likewise found that the mortality rate in 25 ovariectomized females to 400 r total body irradiation was 100 per cent as compared to 48 per cent in 50 control females. They concluded from their work that the influence of the gonadal hormones was most likely due to a side effect stimulating some nongonadal system.

If one makes the assumption, which may or may not be justifiable, that radiation mortality is an extension in degree of radiation morbidity or "radiation sickness," it is interesting to contemplate the comparison between our results in supposedly estrogen-poor human females, and those of the investigators quoted above in ovariectomized female mice.

CONCLUSIONS

1. Forty female patients, receiving external irradiation of the pelvic areas over periods of about a month under certain standardized conditions, form the basis of a study of radiation sickness.

2. In these patients, adrenal cortical reserve, as signified by a modification of the Thorn ACTH-eosinophil four hour response, was found to be within the range of normal initially, but to have fallen considerably below normal at the end of ten to fourteen days. Continued irradiation does not prevent a gradual return of this index of adrenal cortical reserve to normal, or near normal, by thirty to thirty-four days.

3. The basal absolute eosinophil count in these patients, after a slight drop in the first week or so, begins to climb well above normal and reaches its highest point in twenty to twenty-four days, after which a slight return toward normal is noted.

4. A symptom index, derived in uniform fashion from the number and severity of symptoms of radiation sickness found to be present (or absent) in each patient after daily interrogation showed changes parallel to those noted for the absolute eosinophil counts.

5. Consideration of curves established for the above three factors suggests that (a) the adrenal cortex undergoes definite changes in the course of irradiation but these are probably not related to radiation sickness, and (b) that the similarity of the direction of change of the symptom indexes and the absolute eosinophil counts suggests an etiological factor common to both.

6. Evidence is presented to indicate that individuals with presumably low estrogen levels suffer a greater severity of radiation sickness than individuals with evidence of more adequate levels.

7. The literature has been reviewed in regard to the findings of this study and, where possible, comparisons have been established.

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APPENDIX

The differences between the means at the maximum point of each curve in Figure 5 and the initial or control values were found to be statistically significant by the method of Student's t distribution. For the Thorn test $p < .001$; For the basal absolute eosinophil count $p < .001$; For the symptom index, $p = .01$.

A COMPARISON OF THE EFFECTS OF LOCAL ROENTGEN IRRADIATION ON JAW AND TOOTH DEVELOPMENT IN YOUNG AXOLOTLS AND MICE*

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INTRODUCTION

IN PREVIOUS reports, the effect of local roentgen irradiation on the regenerating stumps of amputated parts has been described (Brunst[2]). This was of interest because such regenerating areas normally contain centers of rapid growth and differentiation. It would be of interest to compare the effects of local roentgen irradiation in regenerating limbs or other amputated parts in mammals, but the potentialities for regeneration in these higher forms are very limited. It is, however, possible to select for comparative study of the effect of local roentgen irradiation parts of developing vertebrates that exhibit similar processes and rates of growth and morphogenesis. The jaws of very young animals are especially good for such a study, because the process of tooth formation is essentially the same in most vertebrates. Moreover, by choosing animals of the proper age, one can study not only the effect of local roentgen irradiation on the continuation of growth and development of the jaws and teeth of two widely separated forms, but also the effect of irradiation on previously formed intercellular material and structures such as teeth. At the ages selected for study in these experiments, the jaws of both the axolotls and mice had started the process of developing teeth which were present in various stages of development at the time of irradiation. It will be shown in this paper that the biological effect of local roentgen irradiation to the jaws of very young axolotls and mice is much the same in both of these widely separated forms. In both forms, the growth of jaws was inhibited as was the development of teeth. The most remarkable outcome of these experiments, however, was that the teeth and partially developed teeth present at the time of irradiation disappeared. Roentgen irradiation of the jaws thus destroyed or inhibited not only the mechanism of tooth formation but also the mechanisms of tooth maintenance.

THE EFFECT OF LOCAL ROENTGEN IRRADIATION ON THE JAWS OF AXOLOTLS

Fourteen animals (axolotl—*Siredon mexicanum*, Urodele, Amphibia) were irradiated locally with 2,000–4,000 roentgens at the age of twenty to twenty-two days (after hatching). Twenty-two animals were irradiated with 3,000 r at sixty days of age. During irradiation of the lower jaw, the upper jaw and skull were protected by a small lead plate which was inserted into the mouth of the anesthetized animal. Irradiations were given through a 2 cm. width localizer slit in the protective lead cover which was 4 mm. thick. Irradiations of the upper jaw were given in a similar manner, but from the dorsal aspect. The conditions of irradiation were as follows: 55 kv., 3 ma. max., no filter and 10 cm. target object distance. For histological examination the material was fixed in a saturated solution of bichloride of mercury with 5 per cent acetic acid. It was imbedded in paraffin and sectioned at 10 microns and stained with Böhmer's hematoxylin and eosin.

Observations and Results. The first clear signs of the reaction were observed thirteen days after treatment in the axolotls irradiated with 4,000 r at the age of twenty-two days. In these, the appearance of some

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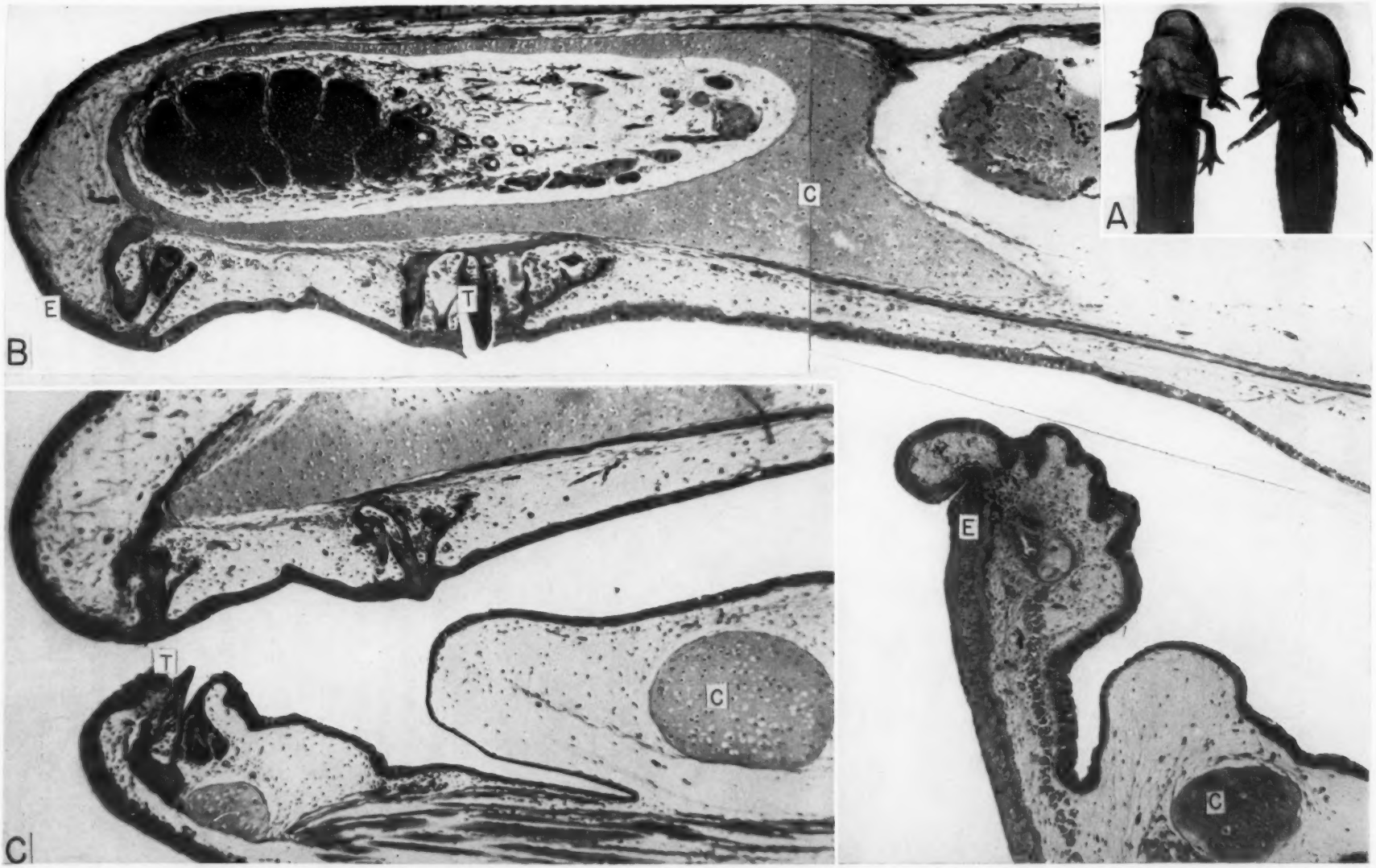


FIG. 1. Suppression of development of lower jaw and teeth of axolotl by roentgen irradiation. (*A*) Irradiated and control animals. Irradiation with 2,000 r of 20 day old animals. Photograph made before fixation for histological examination 110 days after treatment. (*B*) Sagittal section through the upper (not irradiated, control) and lower (irradiated) jaws of the same animal that is shown in (*A*) (left). (*C*) Sagittal section through the upper and lower jaws of control animal shown in (*A*) (right). C, cartilage; E, epithelium; T, tooth. Photomicrograph, ×70.

FIG. 2. Suppression of development of upper jaw and teeth of axolotl by roentgen irradiation. Sagittal section through the upper (irradiated) and lower (control) jaws of an animal 110 days after treatment with 2,000 r of 20 day old animal, C, cartilage; E, epithelium; M, muscle; T, tooth. Photomicrograph, ×70.

areas of the irradiated oral epithelium was not normal. There were many cracks between the cells and abnormal separation of groups of cells. Other parts of the same treated epithelium had a normal appearance. The mitotic activity in the treated tissues had been completely suppressed. The development of teeth and the process of formation of new enamel organs had also been completely arrested in the irradiated jaws.

In the jaws examined twenty-three days after irradiation, a degenerating giant cell epithelium of the treated region was observed. This is a clear sign of the primary acute reaction to irradiation (Brunst;[2,3,4] Brunst, Barnett and Figge[5]). The enamel epithelium associated with developing teeth in the treated region had disappeared, and the resorption of teeth in animals irradiated with 4,000 r was already in progress. Some of the tooth remnants in irradiated jaws were very small and under some of these an accumulation of connective cells

was observed. These cells were in close contact with the tooth and some were fixed in the process of penetrating into the tooth substance. Many of these cells are probably macrophages which play an active part in the process of resorption of teeth.

Thirty-four days after irradiation of the animals with 4,000 r, the resorption of teeth is almost completed. Very small remnants of teeth remain in isolated places of irradiated jaws. It is noteworthy that, at this time, only a slight retardation of growth of the irradiated jaw was observed. It is thus clear that the teeth in the young animals are much more sensitive to roentgen irradiation than is growth of the jaw. The degenerating giant cell epithelium had been replaced with normal epithelium. In spite of the great mitotic activity in this epithelium, it was unable to produce new enamel organs. It is probable that this epithelium developed from the surrounding regions in the periphery of the irradiated field. In any case, it is clear that the competence of the epithelium to develop teeth is limited to a narrow region of the jaw. If this epithelium is destroyed by roentgen irradiation, it may be replaced by new epithelium, but the formation of new teeth does not occur.

By the fifty-eighth day after irradiation all the tissues in the treated jaws appeared normal. The remnants of teeth had disappeared and other teeth failed to develop, even after a long period of time. The mitotic activity was suppressed, and the retardation of growth of irradiated jaws was clearly evident (Fig. 1 and 2). This is a typical reaction of a treated portion of the body to local irradiation which has been described in previous papers and is known as the "stable state" (see Brunst;[2,3,4] Brunst, Barnett and Figge[5]).

THE EFFECT OF LOCAL ROENTGEN IRRADIATION ON THE JAWS OF MICE

The jaws of 60 one to three day old mice were irradiated locally with 2,000–3,000 r. The conditions of irradiation and the method of localization of roentgen rays were the same as those used for the treatment of jaws of axolotls. Irradiation of such young nursing mice was very difficult and a very high mortality was observed after irradiation. In order to obtain definite results, treated mice must be observed for comparatively long periods of time (about 2 months). Only 3 of the irradiated mice survived for this length of time. Two additional mice also survived but did not show any signs of the irradiation effects. It is obvious that these 2 mice were not irradiated because of the technical difficulties of the method. They are not taken into consideration in the results. Such limited material does not make it possible to study the succession of changes which occur in treated parts, but does permit conclusions concerning the effect of the irradiation on the jaws and teeth.

Observations and Results

Experimental Animal No. 18. This mouse was 1 of 6 from the same litter. The jaws of 4 were irradiated with 2,000 r at the age of one day, and 2 served as untreated controls. Sixty-five days after irradiation, only 1 of the irradiated mice was alive. In this mouse, a great suppression of the growth of the lower jaw was observed, and there was a complete lack of teeth in the irradiated jaw. By contrast the incisor of the upper jaw had grown long and sickle shaped because there were no opposing teeth on the lower jaw (Fig. 3, *B*).

Experimental Animal No. 32. This mouse was 1 of a litter of 8. The jaws of 5 mice in this litter were irradiated with 3,000 r at the age of three days and 3 served as untreated controls. One of the 5 irradiated mice lived for sixty-six days after irradiation. In this mouse, the partial suppression of the development of the upper jaw and the absence of teeth were quite evident. The incisors of the lower jaw were abnormally large, as shown in the photographs comparing the experimental and control mice (Fig. 3*A*, *C*).

Experimental Animal No. 56. This mouse was 1 of a litter of 7. The jaws of 5 of these

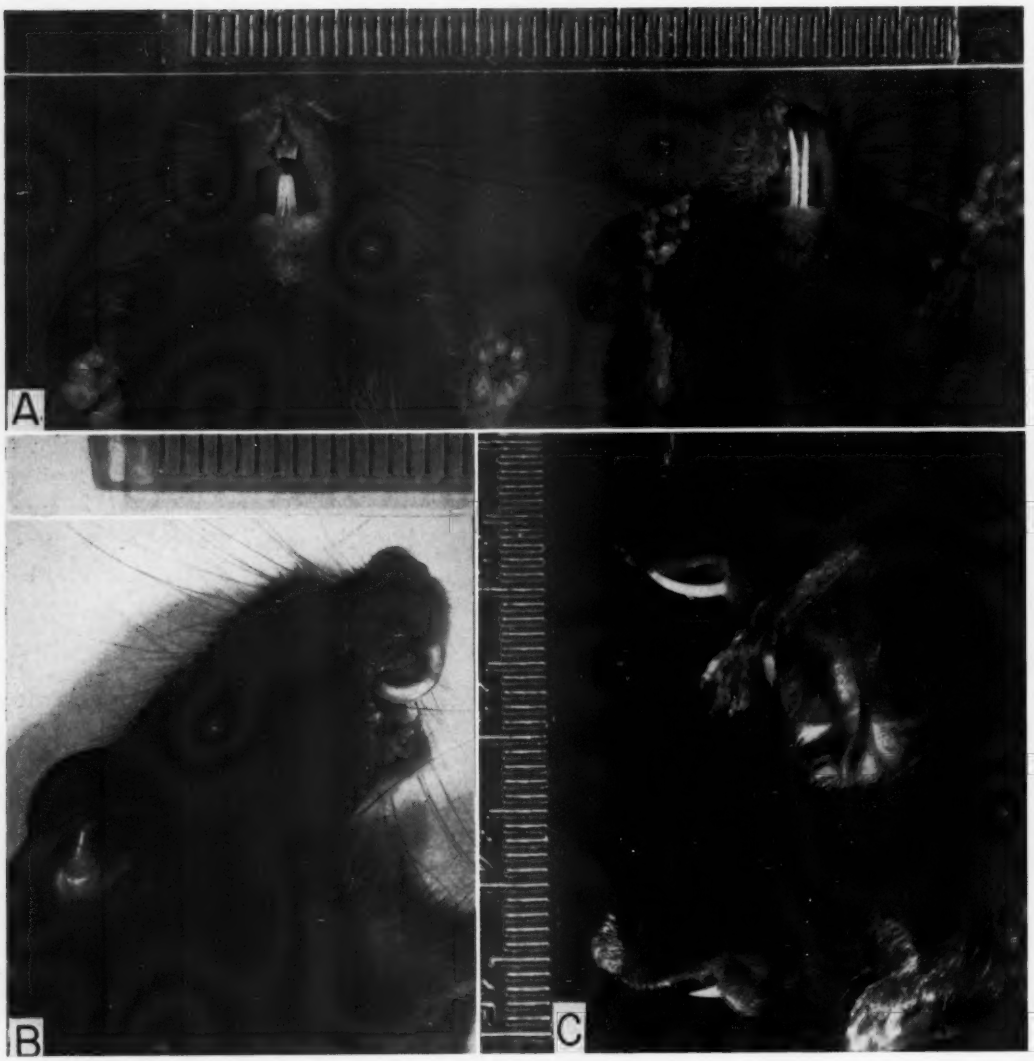


FIG. 3. Suppression of development of jaws and teeth in mouse by roentgen irradiation. (*A*) Control (left) and experimental mouse (right) N 32, 66 days after irradiation of upper jaw with 3,000 r (dorsal view). (*B*) Experimental mouse N 18, 65 days after irradiation of lower jaw with 2,000 r (lateral view). (*C*) Control (lower) and experimental mouse (upper) N 32, 66 days after irradiation of upper jaw with 3,000 r (lateral view).

were irradiated with 2,000 r at the age of two days, and 2 served as untreated controls. Forty-seven days after irradiation, only 1 of the treated mice had survived. This mouse also exhibited partial suppression of growth of the upper jaw and the complete lack of teeth, as seen in other irradiated jaws. The incisors of the lower jaw were, however, approximately normal size. The fact that the incisor of the untreated jaw did not become very large as it did in other animals is not understood. It is possible, however, that this jaw was not entirely protected by the small lead triangle and received some irradiation which might account for the partial inhibition of growth.

Histological examination of jaws of a one day old normal mouse revealed that they have well developed primordia of incisors and molar teeth (Fig. 4*A*, *B*). Formation of dentine and enamel in these teeth anlagen were already in progress. The teeth

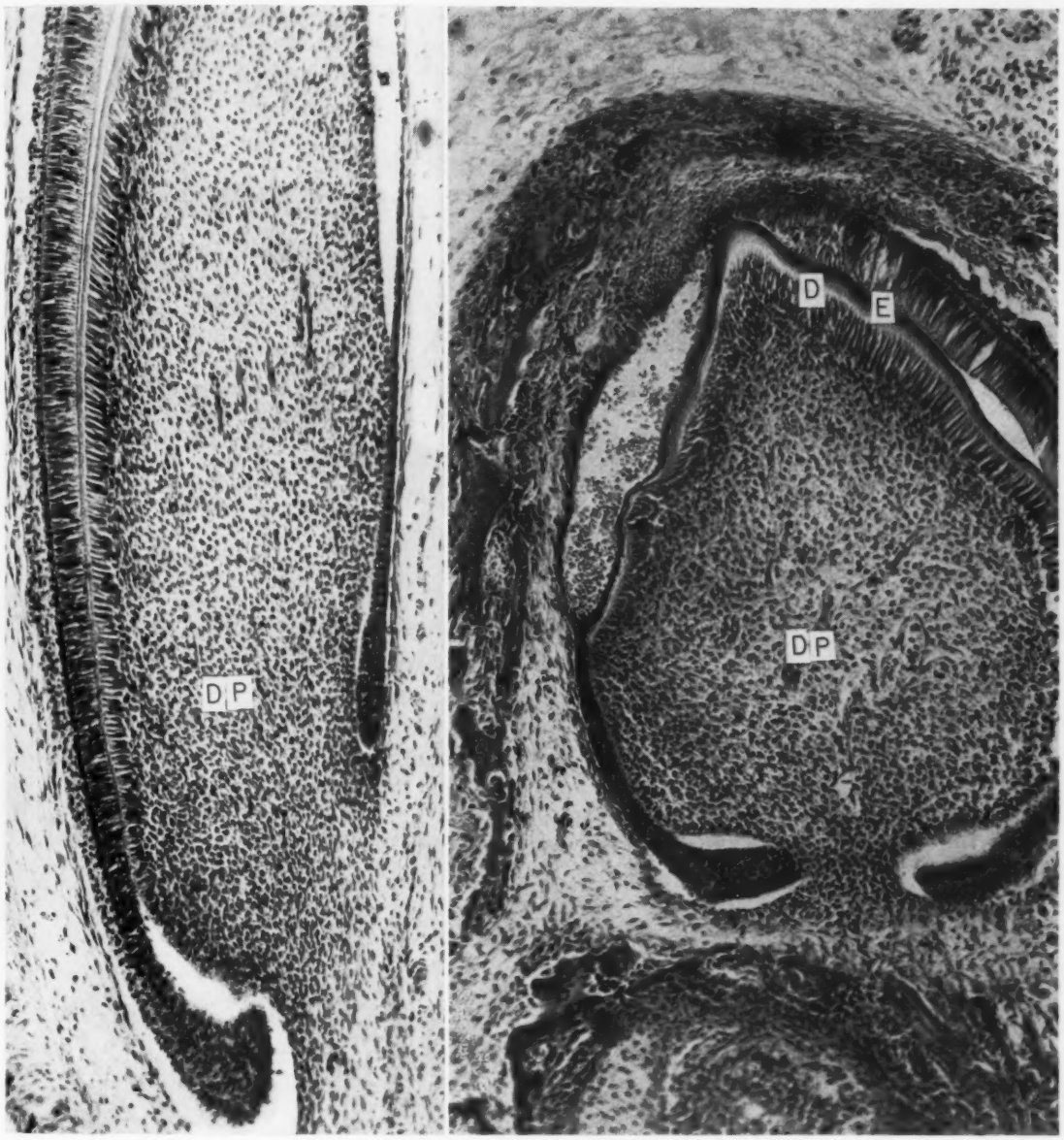
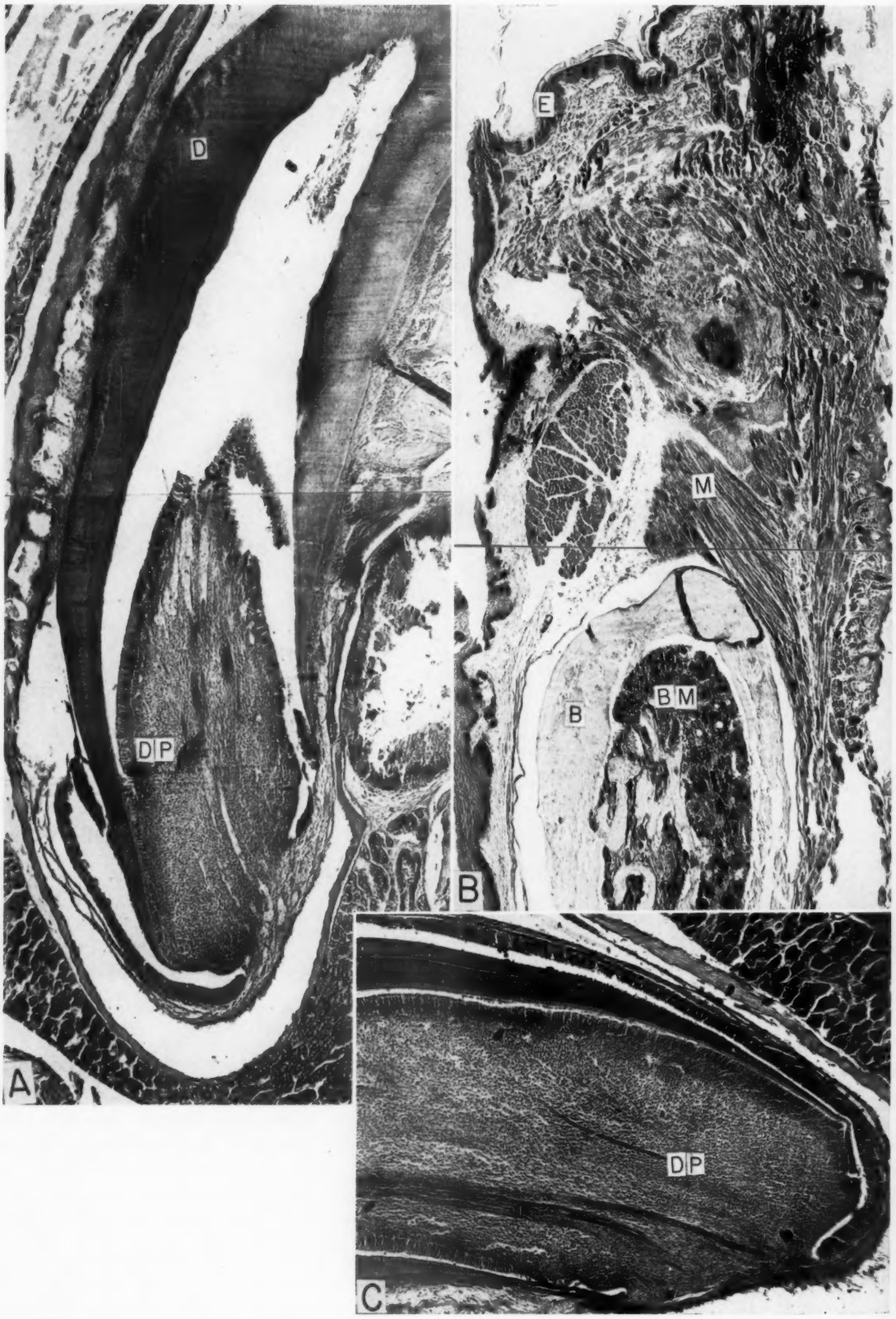


Fig. 4. The teeth anlagen of one day old mouse. Incisor (left) and molar (right). D, dentin; DP, dental pulp; E, enamel. Photomicrograph, ×280.

of two or three day old mice were even more advanced developmentally.

Histological examination of irradiated jaws of experimental animals that had survived for forty-five to sixty-five days after the irradiation revealed that the growth of the treated jaws had been suppressed and that the teeth anlagen or primordia were entirely lacking. In the control nontreated jaws of the same animals the teeth had continued development and had become quite large. The photomicrographs of Figure 5 show a sagittal section through the basal portion of the incisors of the upper or control jaw on the animal described as No. 18 and a similar section through a control animal from the same litter (Fig. 5*A*, *C*). In order to permit comparison of the size of the irradiated jaws of animal No. 18, a photomicrograph at the same magnifica-


D
DP
A
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tion of the sagittal section through the lower irradiated jaw of this animal has been included (Fig. 5*B*). The incisor tooth of the upper jaw was, in fact, as large or larger than the irradiated lower jaw and constitutes a good illustration of the growth inhibitory effects of roentgen irradiation. In accordance with our previous observations, the appearance of the irradiated tissues was normal. This is also another example of the "stable state" which has become established by the sixtieth postirradiation day and persists thereafter (see Brunst;[2,3,4] Brunst, Barnett and Figge[5]). From these histological studies in the mouse and a comparison with the process of disappearance of teeth primordia after roentgen irradiation in axolotls it is obvious that this process is very similar in both. There is some evidence to indicate that the disappearance of the teeth primordia in young axolotls occurs as a result of lysis and phagocytosis. It is possible that a similar process occurs in mice. This process may be secondary to the destruction of cells whose function is to form and maintain the tooth structure.

DISCUSSION

The point which deserves particular emphasis here is that when the developing jaws of two widely separated animals such as the axolotl and the mouse were treated with roentgen irradiation, the biological reaction of both was essentially the same. Both exhibited inhibition with respect to the development of the treated jaw and disappearance of the teeth and teeth primordia. It was noted, however, that there was always a more marked effect in the case of the lower jaw than in the upper jaw. This may be the result of the filtration of the soft roentgen rays as they pass through the skull which is much thicker than the layer of tissues surrounding the lower jaw. This is likely because no filters were used in the irradiation. Therefore, the lower jaw probably receives a greater dosage than the upper jaw.

A number of other investigators have described the effect of roentgen rays on jaws and teeth of mammals. Leist[11,12] noted inhibition of growth of rats' incisors as a result of damage to the odontoblasts. Smith[15] did not find any defects after roentgen irradiation of developing teeth of rats. Herold[10] described inhibition of the growth of jaws and some irregularity and orientation of odontoblasts in the dog's head after irradiation with 1,500 r. Dale[7] studied the effect of roentgen rays on the rat incisor. He irradiated the weanling and adult animals with various doses up to 750 r and observed temporary retardation or cessation of both enamel and dentine formation. Medak, Schour and Klauber[13] described the effects of irradiation on the eruption of the upper incisors in rats weighing 180 to 200 grams. They used doses ranging up to 4,000 r and observed a retardation and cessation of eruption. Weinreb, Schour, Medak and Klauber[16] described the effect of roentgen rays on the growth rate of dentine of the rat incisor in animals weighing from 150 to 200 gm. The growth in length of dentine was stopped abruptly following irradiation with 4,000 r. The growth of dentine in width, however, continued undisturbed. Bruce[1] investigated the effect of radon on the dental system of syrian hamsters, applying the radiation at ages of five to seventy days. This type of irradiation delayed or interrupted the growth of certain teeth as well as the jaws. Burstone and Levy[6] described the effect of 1,500–5,000 r

FIG. 5. Suppression of development of jaws and teeth in mouse by roentgen irradiation. (*A*) Sagittal section through the basal portion of incisor of the upper (not treated, control) jaw of experimental animal N 18. D, dentin; DP, dental pulp. Photomicrograph, ×52. (*B*) Sagittal section through the irradiated lower jaw of the same animal (N 18). B, bone; BM, bone marrow; E, epithelium; M, muscle. Photomicrograph, ×52. (*C*) Sagittal section through the basal portion of the incisor of the upper jaw of control animal. Photomicrograph, ×52.

of roentgen rays on the jaws of mice two to thirty days old. In the irradiated jaws they observed a cessation of normal dentine apposition, and the enamel matrix was poorly formed or absent. In some cases, they noted a hemiatrophy of the mandible. English[8] and English and Tullis[9] investigated the effect of roentgen rays on teeth of swine 157 days old. They noted a hypoplasia of the enamel of the developing molar teeth in animals which received more than 400 r.

To our knowledge, no investigator has described the complete lack of teeth in irradiated jaws such as those described in this paper for axolotls and very young mice. This observation implies not only that tooth development has been stopped by the irradiation, but that this has also resulted in the disappearance of tooth parts which existed at the time of the irradiation. The question arises as to why other investigators have not observed this same phenomenon. From a consideration of the above review of the literature, it is apparent that in some instances other investigators have used such comparatively small doses that the radiation effects cannot be compared with those where higher doses were used. It is also quite probable that in some instances where higher dosages were used, the time interval for postirradiation effects was not long enough to observe changes comparable to those reported in this paper. It is also possible that some of the differences in results may be explained on the basis of species and strain differences, with respect to sensitivity to radiation. However the most important source of the differences in the observations by different investigators stems from the variation in the age sensitivity of tissues to radiation. In other experiments it has been shown that a one day old mouse is much more sensitive to radiation than a five day old mouse (unpublished data). It should therefore be emphasized that the disappearance of teeth and tooth primordia described in this paper was the result of irradiation of very young axolotls and one day old mice.

The problem of age sensitivity to radiation is extremely important. The sensitivity of organisms before birth is even much greater. In spite of the fact that such observations have been described in hundreds of papers, practical roentgenologists have very often ignored this in their work with human subjects. Pregnant women are often subjected to the procedure of taking roentgenograms in three positions and this is, on certain occasions, repeated on the same individual. Russell and Russell[14] think that even the smallest doses which may be received by the pregnant women during diagnostic roentgenoscopy may cause subtle developmental alterations which, in the human subject, would be undesirable.

SUMMARY

Lower or upper jaws of young axolotls at the age of twenty to sixty days were irradiated locally with 2,000–4,000 roentgens. A suppression of the growth of treated jaws was observed in every instance. In the early postirradiation period, a typical degenerating giant cell epithelium was also seen in the irradiated areas of the treated jaws. Fifty-eight days after irradiation, the retardation of the growth of the jaws was clearly evident and all remnants of teeth in them had completely disappeared. In the control (shielded) jaws of the same animals, the development of teeth proceeded normally.

The same kind of experiments were performed with very young mice. The lower or upper jaws of sixty young mice one to three days of age were irradiated locally with 2,000–3,000 r. While a very high mortality was observed after such treatment, three cases survived for a long period of time. In the irradiated jaws of these three animals, there was observed a similar suppression of growth of the irradiated jaws, and there was a complete lack of teeth. This indicated that the teeth and teeth primordia present at the time of the irradiation had disappeared. There is thus a striking similarity in the biological reaction of irradiated jaws in two such widely separated forms as mice and axolotls. The mechanisms of tooth

formation and tooth maintenance were destroyed in both animals by roentgen irradiation.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

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EDITORIALS

PARADOXICAL METASTASIS AND TRANSPULMONARY CANCER SPREAD

IN GENERAL, it is not difficult to explain the location of a metastatic malignancy on the basis of vascular anatomy and circulatory physiology. By contrast, it is often harder to account for the noninvolvement of certain organs. Thus, the lung not infrequently appears free from metastatic deposits in cancers that have invaded the general circulation and in which we should expect pulmonary metastasis. The concept of paradoxical embolism in relation to cancer spread was introduced by Zahn in 1889. He applied it to instances in which the lungs had apparently been bypassed through an open foramen ovale or ventricular septal defect by cancerous emboli, originating in systemic veins and spreading into the general arterial circulation. Zahn based his explanation on Cohnheim's earlier demonstration (1877) of interatrial or interventricular defects in cases in which simple or infectious thrombi, arising in the veins of the lower extremity, had been propagated embolically into the arterial circulation, *e.g.*, of the brain, without involvement of the lungs. Modern authors agree that the evidence in support of the theory of paradoxical embolism is rather unconvincing and advance other explanations for atypical cancer spread to the skeleton, such as occurs in prostatic or mammary cancer with apparent noninvolvement of the lungs.

In 1936, Warren, Harris and Graves, on the basis of detailed histologic studies, pointed to the perineural lymphatics in the neighborhood of the prostate as an important channel of metastatic tumor dissemination to the most commonly involved bones: the pelvis, sacrum, and lumbar vertebrae. Turner has come out strongly in support of this pathway in the spread of prostatic malignancy, in preference to more recent explanations of the hematogenous origin of vertebral involvement.

A great deal of attention has been given lately to the metastatic pathway along the veins of the vertebral plexus, first suggested by Batson in 1940. While this rich and complex venous network within and outside the spinal canal has been known for more than a century, Batson postulated, on the basis of his injection experiments, that this is the channel along which cancerous emboli travel from the prostate to the pelvis, the spinal column and skull, and also from the breast to the skeleton, in both cases bypassing the lungs. Further confirmation of this mode of dissemination came from Coman and de Long who subjected Batson's hypothesis to an experimental test in laboratory animals. Batson had previously demonstrated on monkeys that it required some increase in intra-abdominal pressure to divert part of the blood flow from the caval system into the vertebral plexus. Following this suggestion, Coman and de Long applied moderate pressure to the abdomen of rabbits and rats while they injected a suspension of carcinoma cells into their femoral vein. When the animals were sacrificed, they displayed numerous metastases in the lumbar vertebrae apparently arising from cancerous emboli in the vertebral veins. The arterioles were shown to be free from metastasis. Control animals, in which no abdominal compression had been applied, revealed metastatic emboli and tumors only in the lungs. Recently, Franks in Britain combined the roentgenologic and

histologic approach and injected a barium suspension into the dorsal vein of the penis of human cadavers. He then demonstrated the medium roentgenographically and microscopically in the venous plexus around the prostate and lumbar vertebrae. He showed opaque material and cancerous emboli lying side by side in a prostatic vein and also depicted roentgenographically barium-filled veins within an osteoplastic metastasis. So far no cancerous emboli have actually been demonstrated in humans within the veins of a skeletal metastasis, other than the prostate itself. This evidence would supply the final link in this chain of arguments in favor of the venous, instead of the lymphatic or arterial origin of vertebral metastasis, particularly if the absence of emboli in the arterioles could be proved at the same time.

On the other hand, the followers of the theory which ascribes metastatic involvement of the skeleton to generalized arterial spread can also derive support from the recent literature. One of the most forceful arguments of proponents of the vertebral venous plexus as pathway in the spread of prostatic and mammary cancer is the not infrequently noted absence of pulmonary metastasis in the presence of skeletal dissemination. This seems to be proof that the pulmonary filter, which is located at the headwaters of the arterial stream, has not been traversed by cancerous emboli. For some time, considerable doubt has been cast on this evidence for several reasons. First of all, noninvolvement of the lung on gross inspection does not prove actual absence of metastases. The latter may be of microscopic size and still give rise to further spread. Thus, in Walther's first series of metastasizing prostatic cancer, there was reported a 35 per cent absence of lung involvement at autopsy. This figure was reduced to 6 per cent in his later series, when special attention was paid to the lung by searching for microscopic spread in numerous sections from all portions of the organ. While the number of misses naturally would be considerably larger than even Walther's first figure, if exclusion of lung involvement were based on roentgen evidence alone, careful roentgenographic search might increase the number of clinically diagnosed cases of pulmonary involvement. This would be particularly true if sectional radiography of the lung were included in the study (Kane).

In a classical publication M. B. Schmidt, as early as 1903, and later Stern, and most recently Saphir, have pointed out, on the basis of histologic evidence, that cancerous emboli in the pulmonary arterial system may be destroyed through organization of their thrombotic enclosure. It is certainly conceivable that these emboli may have given rise to generalized dissemination in the systemic circulation, before they were made innocuous in the lung by organization of the thrombi that had encapsulated them. In that case there would be no gross and little microscopic evidence of their former activity in the lung. According to Saphir, the histopathologic picture might closely resemble pulmonary arteriosclerosis.

The most common mode of spread from the lungs into the systemic circulation is probably by means of a double breakthrough of the pulmonary vascular system. The cancerous embolus, once arrested in a pulmonary artery or arteriole, may, if it remains viable, penetrate through the vascular wall with development of a florid pulmonary metastasis. This is particularly apt to occur if the break-through takes place into the perivascular lymphatics, which form a favorable nidus for malignant cells. The process may readily be followed later by cancerous invasion of a pulmonary vein and dissemination via the left heart into the general arterial circulation. In rarer cases the pulmonary vascular system might be permeated by cancerous thrombi, the cancerous plug starting in the arterioles and growing by continuity through the capillaries into the pulmonary venous system, spread from there through the heart into the arterial blood (Stern).

The final and most important question

that unavoidably occurs to everyone attempting to explain the location of systemic metastases in the presence of noninvolvement of the lungs is, of course: Does transpulmonary passage of cancerous emboli occur? In other words, to what extent is the pulmonary filter a leaky filter, permitting cancer cells to pass through? This raises the subsidiary query as to the minimum size of a malignant embolus capable of causing dissemination. If the channel for the passage of tumor cells goes by way of the pulmonary capillaries into the pulmonary veins and from there into the arterial system, only single and small-sized malignant cells would be able to traverse this narrow pathway. Most authors agree that this is quite unlikely (Walther, Willis). Lawrence and his co-workers recently quoted a figure of six cancer cells as a critical-sized colony for successful growth. Boyd supports the view, also expresssed by Willis, that metastases are caused by clumps of tumor cells rather than individual cells—clumps that are too large to pass through the capillary system.

Here the recent observations of Prinzmetal and his co-workers, of Tobin and Zariquiey, and of von Hayek supply the answer. These authors have shown either by direct histologic studies (von Hayek), or through physiologic experiments by means of perfused glass beads of varying size (Prinzmetal *et al.*), or by a combination of the latter method with direct and roentgenographic observation of the injected human lung (Tobin and Zariquiey), that there exist in the lung shunts between pulmonary arteries and veins, bypassing the capillary circulation, of a size up to 500 microns in diameter. These shunts are located in the parenchyma of the lung, in the bronchial wall and subpleurally. They would permit fair-sized multicellular emboli to pass though the lungs without arrest. The passage of parasitic ova such as those of schistosomes has been explained on the same anatomic basis (Brink).

Zeidman and Buss have recently approached the problem of transpulmonary passage of tumor cell emboli by animal experiments. Suspensions of cells of three different types of tumors were injected into the ear veins of rabbits and rats and their aortic blood recovered immediately after injection. This blood was then re-injected intravenously into a second animal of the same species where it produced tumors. The experiments showed that cells of all three types of malignancy were able to pass through the lung without delay. In one type, the Brown-Pearce rabbit carcinoma, the transpulmonary passage was more readily executed than in the other two types. In five cases of the former type, the tumor cells apparently succeeded in passing through the lungs of two animals without arrest, causing peripheral metastases in the second animal. The reason for the difference in the incidence of transpulmonary passage in the three types is not quite clear, but does not lie in variations of cell size. The authors suggest greater viability and pliability of one type as an explanation. Lawrence and his co-workers, in their experiments on V_2 rabbit carcinoma, were able to pass the lung barrier by the application of heparin, ascribing the pulmonary arrest of the cancerous emboli, that otherwise occurred, to the thromboplastic activity of the tumor.

In the light of the available evidence, we must assume that cancer, like erupting lava, will not confine itself to one channel, but will choose any available pathway to reach its final destination.

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DARMON A. RHINEHART
1887-1954

DR. DARMON A. RHINEHART of Little Rock, Arkansas, Professor Emeritus of Radiology at the University of Arkansas School of Medicine, died on Saturday evening, May 22, 1954, at his home.

Dr. Rhinehart was born in Indiana in 1887. He received his Bachelor's, Master's, and Doctor's degrees from Indiana University and served as instructor in anatomy before moving to Little Rock, Arkansas, where he taught anatomy in the University of Arkansas and was head of that department. He later took up radiology and established the first Department of Radiology at the University of Arkansas and for a time continued to teach in both departments.

Dr. Rhinehart was a Past President of the Arkansas Medical Society; Chairman of the Section of Radiology of the Southern Medical Association; a Diplomate of the American Board of Radiology; a Fellow of the American College of Radiology; and a Past President and Member of the Board of Trustees of the American Registry of X-ray Technicians. He was a member of the Free and Accepted Masons, Consistory, Scimitar Shrine, Rotary, Country Club and Riverdale Club, all of Little Rock, Arkansas.

Both in the practice of his profession and as a teacher, Dr. Rhinehart made a firm place for himself. For the years that strength remained to him he gave valuable service in both fields. The distinction that he won in the branch of medical science to which he devoted himself is impressively told by the honors that came to him. His passing is a loss to the medical profession and to the citizens of Little Rock.

IRA H. LOCKWOOD, M.D.

Resolutions Passed by the Arkansas Radiological Society

WHEREAS, Darmon Artelle Rhinehart departed this life May 22, 1954, and

WHEREAS, As a practicing physician and roentgenologist he cherished and espoused the highest ideals of the medical profession, ever mindful of the rights and interests of the patient and the physician, and

WHEREAS, He was enthusiastic in the activities of medical organizations, county, state, and national, and in the various specialty societies,

THEREFORE, BE IT RESOLVED, That the Arkansas Radiological Society adopt this resolution of respect to his memory.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 21–24, 1954.

American Radium Society
Secretary, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: Shoreham Hotel, Washington, D. C., April 21–23, 1955.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Biltmore Hotel, Los Angeles, Calif., Dec. 5–10, 1954.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich.

Fifth Inter-American Congress of Radiology
Secretary-General, Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa. Meets at Shoreham Hotel, Washington, D. C., April 24–29, 1955.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

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Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary. Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

Colorado Radiological Society
Secretary, Dr. Parker Allen, Children's Hospital, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. B. B. Alicandri, 20 Maple St., Springfield, Mass. Meets second Friday October and April.

Dallas-Fort Worth Radiological Club
Secretary, Dr. O. H. Grunow, 650 Fifth Ave., Fort Worth, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, Oct. through May, at David Whitney House, 4421 Woodward Ave., at 6:30 P.M.

East Bay Roentgen Society
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Florida Radiological Society
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Georgia Radiological Society
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Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. John A. Robb, 238 Hume-Mansur Bldg., Indianapolis 4. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary Dr. A. M. Cherner, Hays, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. David Shapiro, 323 East Chestnut St., Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Solomon Maranov, 1450 51st St., Brooklyn 19, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. Oscar Harvey, 3741 Stocker St., Los Angeles 8, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. Jack Spencer, Maine General Hospital, Portland 4, Maine. Meets in early spring, June and fall.

MARYLAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Paul W. Roman, 1810 Eutaw Place, Baltimore 17, Maryland.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Meets at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Frank Huber, Hempstead, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Sidney Rubenfeld, 477 First Ave., New York 16, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Sternbergh, Charlotte Memorial Hospital, Charlotte, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTH FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. Ivan Isaacs, 1485 Cheshire Road, Jacksonville, Florida. Meets quarterly in March, June, September and December.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. D. H. Baxter, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. M. M. Thompson, Jr., 319 Toledo Medical Bldg., Toledo 2, Ohio.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. F. C. Shipps, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Raines, 214 Medical-Dental Bldg., Portland 5, Oregon. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse 416 Pine St., Williamsport. Next annual meeting at Berkshire Hotel, Reading, Penna., May 20 and 21, 1955.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets second Wednesday of month, October through June at Hotel Roosevelt.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Chapin Hawley, 927 Carew Tower, Cincinnati 2, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Dr. P. S. Arthur, Young Hotel Bldg., Honolulu 13, T. H. Meets third Friday of each month at a place designated by the Secretary.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. J. T. Brierre, 700 Audubon Bldg., New Orleans. Meets annually during Louisiana State Medical Society Meeting.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Carye-Belle Henle, 195 North 7th St., Newark, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Henry H. Forsyth, Jr., 40 Meigs St., Rochester, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Freed, 4200 East Ninth St., Denver 7, Colo. Meets at Shirley-Savov Hotel, Denver, Colo., Aug. 19–21, 1954.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. W. B. Seaman, 510 South Kingshighway, St. Louis 10, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Antonio-Military Radiological Society
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

San Diego Radiological Society
Secretary, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

Section on Radiology. California Medical Association
Secretary, Dr. H. R. Morris, 1027 "D" St., San Bernardino, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary, Dr. John A. Long, 1801 K St., N.W., Washington 6, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M. September to May inclusive.

South Bay Radiological Society
Secretary, Dr. J. J. McCort, Santa Clara County Hospital, San Jose, Calif. Meets second Wednesday each month.

South Carolina Radiological Society
Secretary, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. G. K. Henshall, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

Tri-State Radiological Society
Secretary, Dr. S. N. Tager, 219 Walnut St., Evansville, Ind. Meets last Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks' Club in Evansville.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Eva L. Gilbertson, 1317 Marion St., Seattle 4, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

West Virginia Radiological Society
Secretary, Dr. W. Paul Elkin, 515 Medical Arts Bldg., Charleston, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. M. G. Priestman, New Rochelle Hospital, New Rochelle, N.Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday, at 7:45 P.M., Lane Hall, Stanford University Hospital.

Cuba, Mexico, Puerto Rico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiología, A. C.
Secretary General, Dr. Eugenio Toussaint, Calle del Oro No. 15, Mexico 7, D.F. Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. Rafael A. Blanes, Ave. Ponce de Leon 1175, Santurce, P. R.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

Association of Radiologists of the Province of Quebec
Secretary, Dr. J.-P. Jean, 4039 Tupper St., Westmount, Que.

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicales
General Secretary, Dr. Ls Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL CENTRO SEDE, CORDOBA
President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DEL NORTE, SEDE, TUCUMAN
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

SOCIEDAD ARGENTINA DE RADIOLOGIA, FILIAL DE CUYO SEDE, MENDOZA.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

SOCIEDADE BRASILEIRA DE RADIOLOGIA MEDICA
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

SOCIEDADE BRASILEIRA DE RADIOTERAPIA
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

SOCIEDAD COLOMBIANA DE RADIOLOGIA
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6° piso, Bogota, Colombia. Meets last Thursday of each month.

SOCIEDAD PERUANA DE RADIOLOGIA
Secretary, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

SOCIEDAD DE RADIOLOGICA, CANCEROLOGIA Y FISICA MEDICA DEL URUGUAY
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

CONTINENTAL EUROPE

SOCIÉTÉ BELGE DE RADIOLOGIE
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

SOCIÉTÉ FRANÇAISE D'ELECTRO-RADIOLOGIE MÉDICALE, and its branches: SOCIÉTÉ DU SUD-OUEST, DU LITTORAL MÉDITERRANÉEN, DU CENTRE ET DU LYONNAIS, DE L'OUEST, DE L'EST, ET D'ALGER ET D'AFRIQUE DU NORD
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX°, France.

CESKOSLOVENSK SPOLEČNOST PRO RÉNTGENOLOGII A RADIOLOGII V PRAZE
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

DEUTSCHE RÖNTGEN-GESELLSCHAFT
Secretary, Dr. med. Peter Kröker, Evangelisches Krankenhaus, Huyssens Stiftung, (22a) Essen. Annual meeting, Sept. 5–8, 1954, Wiesbaden, Germany.

SOCIETA ITALIANA DI RADIOLOGIA MEDICA
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

NEDERLANDSE VERENIGING VOOR ELECTROLOGIE EN ROENTGENOLOGIE
Secretary, Dr. B. J. Rethmeier, Bornsestraat 378, Almelo, Netherlands.

POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

GDANSK SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept., Akademia Gdansk.

WROCŁAW SECTION, POLISH SOCIETY OF RADIOLOGY
Secretary, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SOCIEDAD ESPANOLA DE RADIOLOGIA Y ELECTROLOGIA
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

SCHWEIZERISCHE RÖNTGEN-GESELLSCHAFT (SOCIÉTÉ SUISSE DE RADIOLOGIE)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

INDIA

INDIAN RADIOLOGICAL ASSOCIATION
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

GRANTS AND AWARDS IN RADIOLOGICAL RESEARCH OF THE JAMES PICKER FOUNDATION

The James Picker Foundation has announced the award of nine Grants and two Fellowships in Radiological Research for the coming year. These awards, totaling approximately $42,000, were made on recommendation of the Committee on Radiology of the National Academy of Sciences–National Research Council.

The Picker Foundation was established in 1947, with the objective of fostering research in and broadening the scope of radiology. With the cooperation of the Academy–Research Council, the Foundation initiated its program of research grants and fellowships in 1950. Since that time, grants have been made in support of investigations in nine laboratories in this country and in three foreign institutions. An additional grant has been made for support of a Scholar in Radiological Research, and fellowships have been awarded to four young scientists to enable them to advance their preparation for investigative careers in the field of radiology.

Grants in Radiological Research for 1954–1955 have been made to the following investigators:

Dr. Henry Doubilet, New York University College of Medicine, for continued work on the x-ray visualization of the biliary and pancreatic ducts.

Dr. Jack Friedman, Mount Sinai Hospital, Minneapolis, for studies on the effect of emotion on the mucosal pattern of the small bowel.

Dr. J. W. Grossman, and Dr. J. L. Howarth, Lovelace Foundation for Medical Education and Research, Albuquerque, for development of techniques for dose estimation, using a Cobalt-60 unit.

Dr. George Jacobson and Dr. Donald C. Balfour, Jr., University of Southern California School of Medicine, for an investigation of the use of pharmacological agents in the radiologic diagnosis of gastrointestinal disease.

Dr. Hilde Levi, Zoophysiological Laboratory, University of Copenhagen, for continuation of her autoradiographic studies of alpha and soft beta emitters in animal tissue.

Dr. Gardner Middlebrook, National Jewish Hospital, Denver, for continued pulmonary angiographic studies pre- and post-resection in tuberculosis and simulating diseases.

Dr. Bjorn E. W. Nordenstrom, Sabbatsberg Hospital, Stockholm, for continuation of his work on the development of a new principle for examination by x-ray of pulmonary vessels.

Dr. Henry P. Plenk, University of Utah College of Medicine, for continued studies on the influence of drugs on radiation reaction.

Dr. William J. Tobin, Georgetown University School of Medicine, for continued study of bone architecture.

The following have been awarded Fellowships in Radiological Research for the coming year:

Dr. Murray G. Smyth, Jr., for studies on the distribution and dosage of colloidal and particulate sources of radioactivity, under the guidance of Dr. R. H. Chamberlain at the University of Pennsylvania School of Medicine.

Dr. Kakarla Subbarao, for an investigation of regional ileus as a roentgenological manifestation of disease, under the guidance of Dr. M. H. Poppel at the Bellevue Hospital, New York.

MEDICAL RESEARCH FELLOWSHIPS

The Division of Medical Sciences of the National Academy of Sciences–National Research Council is accepting applications for postdoctoral research fellowships for 1955–1956. These awards are designed to offer research experience for promising individuals who look forward to investigative careers, and not to provide practical experience in the clinical field. Ordinarily Fellowships are not granted to persons over thirty-five years of age. The following programs are announced:

Fellowships in Cancer Research are awarded by the American Cancer Society on recommendation of the Committee on Growth of the Division of Medical Sciences. Awards are available for study in all branches of the biological, chemical and physical sciences and of clinical investigation applicable to the study of growth, typical or malignant. Citizens of the United States are eligible.

British-American Exchange Fellowships in Cancer Research also are awarded by the American Cancer Society upon recommendation by the Committee on Growth. They are offered to citizens of the United States for advanced study in Great Britain in specialized fields pertaining to the problem of growth. Similar fellowships are awarded by the British Empire Cancer Campaign to young British scientists for research in the United States.

Fellowships in the Medical Sciences, supported by The Rockefeller Foundation and by The Lilly Research Laboratories, are administered by the Medical Fellowship Board of the Division. Fellows are expected to devote themselves to research in the basic medical sciences. The

Fellowships administered for The Rockefeller Foundation are open to citizens of the United States and Canada; the Lilly Fellowships only to citizens of the United States.

Fellowships in Tuberculosis are also administered by the Medical Fellowship Board under a grant from the National Tuberculosis Association. These awards are designed to promote the development of investigators in fields related to tuberculosis. They are open to citizens of the United States who are graduates of American schools.

Fellowships in Radiological Research are administered for the James Picker Foundation by the Division's Committee on Radiology. The Foundation has expressed particular interest in the support of candidates who propose to carry on research oriented toward the dignostic aspects of radiology. Appointments are not limited to citizens of the United States.

Applications for 1955–1956 under any ofthese programs must be postmarked on or before *December 10, 1954*. Fellowships are awarded in the early Spring. Complete details and application blanks may be obtained from the Fellowship Office, National Academy of Sciences–National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D.C.

GRANTS AND FELLOWSHIPS IN RADIOLOGICAL RESEARCH OF THE JAMES PICKER FOUNDATION

On behalf of the James Picker Foundation, the National Academy of Sciences–National Research Council announces the continued availability of funds in support of radiological research. Applications are reviewed by the committee on Radiology of the Academy–Council's Division of Medical Sciences. Final determination of awards is made by the Foundation upon recommendation of the Committee. The Foundation has expressed particular interest in the support of studies oriented toward the diagnostic aspects of radiology. Awards are not restricted to citizens of the United States.

Grants-in-aid are designed to encourage research offering promise of improvement in radiological methods of diagnosis or treatment of disease. Applications for grants-in-aid for the fiscal year 1955–1956 must be submitted on or before November 30, 1954.

Grants for Scholars are a transitional form of support, designed to bridge the gap between the completion of fellowship training and the period when the young scientist has thoroughly demonstrated his competence as an independent investigator. A grant of $6,000 per year will be made directly to the Scholar's institution as a contribution toward his support, or his research, or both. Initial grants are limited to one year, but renewal may be recommended. Applications for 1955–1956 should be submitted by the institution on behalf of the candidate prior to November 30, 1954.

Fellowships in Radiological Research, available under the program of the Foundation, have been announced separately.

Further details and application blanks may be obtained from the Division of Medical Sciences, National Academy of Sciences–National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D. C.

UROLOGY AWARD

The American Urological Association offers an annual award of $1000 (first prize of $500, second prize $300 and third prize $200) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been graduated not more than ten years, and to men in training to become urologists.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Biltmore Hotel, Los Angeles, California, May 16–19, 1955.

For full particulars write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Maryland. Essays must be in his hands before January 1, 1955.

Committee on Scientific Research
Miley B. Wesson, *Chairman*
Harry M. Spence
Vincent J. O'Conor

BLOOD COUNTS

STATEMENT OF NATIONAL COMMITTEE ON RADIATION PROTECTION

An ad hoc committee of the National Committee on Radiation Protection was formed two years ago for the purpose of determining whether or not the use of blood count techniques was necessary in the control of radiation exposure. The following statement has been prepared by the subcommittee and adopted by the National Committee on Radiation Protection:

"1. Provided that radiation monitoring of personnel, and where applicable of sites, is

carried out by instruments (film badges, pocket meters, etc.) in all circumstances involving potential exposure to penetrating ionization radiations, blood counts should no longer be required as a METHOD OF MONITORING.

"2. Blood counts as a part of pre-employment, interval, and terminal examinations are good medical practice—to be done at the discretion of the medical officer in charge—but not as a part of a monitoring service.

"3. Blood counts are a necessary part of the medical examination of anyone over-exposed to penetrating ionizing radiations."

STATUS OF CANCER KNOWLEDGE IS SUITER LECTURE TOPIC

Six authorities on cancer will participate in the 1954 A. Walter Suiter Lecture, November 4, 1954, at The New York Academy of Medicine, in the form of a symposium entitled "Cancer: What We Know Today."

The program, which is planned particularly to give the general practitioner a well rounded view of the present status of knowledge about cancer, has four parts. The first three topics and the speakers will be:

Changing Incidence of Cancer over the Years. Harold F. Dorn, Ph.D., Chief, Office of Biometry, National Institutes of Health, Bethesda, Maryland.

Multiple Views on the Causation of Cancer. Dr. Harold L. Stewart, Chief, Laboratory of Pathology, National Cancer Institute, Bethesda, Md.

The Natural History and Diagnosis of Cancer. Dr. Lauren V. Ackerman, Professor of Surgical Pathology and Pathology, Washington University School of Medicine, St. Louis.

The fourth topic will be "Modern Therapeutic Measures in Cancer and Their Effectiveness," with the following speakers:

Surgery. Dr. Owen H. Wangensteen, Professor of Surgery, University of Minnesota Medical School, Minneapolis.

Radiology. Dr. Richard H. Chamberlain, Associate Professor of Radiology, University of Pennsylvania School of Medicine, Philadelphia.

Chemotherapy. Dr. Alfred Gellhorn, Director, Institute of Cancer Research, Columbia University College of Physicians and Surgeons, New York.

The Suiter Lecture is presented under the auspices of the Academy's Committee on Public Health Relations, to which Dr. Suiter at his death in 1925 left a legacy to finance lectures in public health or legal medicine, his two principal personal interests. For this symposium the New York City Cancer Committee is cooperating with the Committee on Public Health Relations.

Dr. Suiter, a native of Herkimer, New York, graduated from Columbia University College of Physicians and Surgeons in 1871 and spent his life practicing in Herkimer. He was greatly concerned with medical jurisprudence, having served as an expert in both civil and criminal cases. He was among those instrumental in the establishment of the state board of medical examiners and served as a member of the board for several years. In public health he took particular interest in problems of municipal sanitation.

CONFERENCE ON ELECTRICAL TECHNIQUES IN MEDICINE AND BIOLOGY

For several years, the American Institute of Electrical Engineers, Committee on Electrical Techniques in Medicine and Biology, have sponsored an Annual Technical Conference. Co-sponsors are the Institute of Radio Engineers and the Instrument Society of America. The objective of this Conference is to provide a common meeting place for the presentation and discussion of pertinent ideas from electrical and electronic workers and those who make use of these techniques in the field of experimental medicine and biology.

This year the Conference on Electrical Techniques in Medicine and Biology will be held at the Morrison Hotel, Chicago, Illinois, November 10 and 11, 1954. The Chairman is Mr. E. Dale Trout, 4855 Electric Avenue, Milwaukee 1, Wisconsin.

FIFTH INTER-AMERICAN CONGRESS OF RADIOLOGY

The Fifth Inter-American Congress of Radiology which will be held at the Shoreham Hotel in Washington, D. C., April 24 to 29, 1955, offers an extraordinary opportunity for graduate education. Immediately before the meeting of the Congress the American Radium Society will hold its annual meeting in the same hotel, and immediately following the Congress there will be a short refresher course on radioactive isotopes offered by the National Cancer Institute.

Thus it will be possible to spend approximately ten days in a scientific atmosphere, which should be very rewarding to every participant, and it is anticipated that a great many radiologists from Latin America, from Canada and

from the United States will wish to take advantage of this unusual combination of scientific events.

During the meeting of the Congress itself there will be featured refresher courses on various subjects offered both in Spanish and in English. These courses will be given by outstanding specialists in the various fields and will surely prove to be of great benefit.

About 1200 rooms have been reserved at the Shoreham and Wardman Park Hotels and every one who contemplates attending the Congress is urged to apply at once for membership in the Congress to secure hotel reservations.

Applications for membership in the Congress and all general communications should be addressed to the Secretary-General, Dr. E. P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pennsylvania.

GEORGIA RADIOLOGICAL SOCIETY

At the May, 1954, meeting of the Georgia Radiological Society the following officers were elected for the coming year: *President*, Dr. Franklin G. Eldridge, Valdosta; *Vice President*, Dr. William Coles, Atlanta; *Secretary-Treasurer* Dr. Herbert M. Olnick, 417 Persons Bldg., Macon, Georgia. The next meeting will be a joint meeting with the Florida State Association in November, 1954.

NEW ENGLAND ROENTGEN RAY SOCIETY

At the Annual Meeting of the New England Roentgen Ray Society, held at the Hotel Shelton, Boston, on May 15, 1954, the following officers were elected for the coming year: *President*, Dr. Jack Spencer, Portland, Maine; *Vice President*, Dr. Felix G. Fleischner, Boston, Massachusetts; *Secretary*, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Massachusetts; *Treasurer*, Dr. Magnus I. Smedal, Boston, Massachusetts.

The meeting place for 1954–1955 will be the Hotel Commander, Cambridge, on the third Friday of each month at 4:30 P.M.

NEW YORK ROENTGEN SOCIETY

The following officers of the New York Roentgen Society have been elected for the year 1954–1955: *President*, Dr. Harold W. Jacox; *Vice President*, Dr. Jacob R. Freid; *Secretary*, Dr. Sidney Rubenfeld, 477 First Ave., New York 16, New York; *Treasurer*, Dr. Maxwell H. Poppel.

OREGON RADIOLOGICAL SOCIETY

At the last monthly meeting of the Oregon Radiological Society the following were elected as the new officers for the coming year: *President*, Dr. C. Todd Jessell, Portland; *President-Elect*, Dr. Gregory B. Nichols, Portland; *Vice President*, Dr. Clay A. Racely, Eugene; *Secretary-Treasurer*, Dr. Fred C. Shipps, 214 Medical-Dental Bldg., Portland 5, Oregon.

PENNSYLVANIA RADIOLOGICAL SOCIETY

The newly elected officers of the Pennsylvania Radiological Society for the year 1954–1955 are as follows: *President*, Dr. George W. Chamberlin, Reading; *President-Elect*, Dr. William T. Rice, Rochester; *First Vice President*, Dr. Mark K. Gass, Sunbury; *Second Vice President*, Dr. Lea A. Cobbs, Salem, Ohio; *Editor*, Dr. Carl B. Lechner, Erie; *Secretary-Treasurer*, Dr. James M. Converse, 416 Pine Street, Williamsport, Pennsylvania.

The next annual meeting of the Pennsylvania Radiological Society will be held at the Berkshire Hotel, Reading, Pennsylvania, on May 20 and 21, 1955.

Vol. 72, No. 3

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Symposium Neuroradiologicum, Stockholm. *Acta radiol.*, Aug.–Sept., 1953, *40*, 85–370.

The Third Symposium Neuroradiologicum was held in Stockholm, September 17–20, 1952. Dr. Erik Lindgren, in his introductory remarks, traced the history of these meetings which are planned as symposia rather than congresses so "that every speaker must have the time he desires at his disposal" and a more liberal exchange of views can follow the presentation of the subject. The First Symposium was arranged in 1939 in Antwerp with Thienpont presiding. The meeting was so successful that the participants, at the suggestion of Erik Lysholm, decided to convene again within a few years in Holland. However, soon World War II broke out and this plan had to be temporarily postponed. Finally, ten years later, in 1949, the Second Symposium was held in Rotterdam. By that time, both Thienpont and Lysholm had died and the presidency was entrusted to Dr. Ziedses des Plantes. Twenty-four papers were read at this Second Symposium and the results achieved were again most satisfactory.

The honor of President of the Third Symposium Neuroradiologicum was conferred upon Dr. Erik Lindgren who through untiring efforts arranged an admirable program. Thirty-two papers were read, dealing with all the important phases of present-day neuroradiological investigations and a number of illustrious scientists took part in the discussions which followed. The main topics included in the program were: I. Angiography: (A) vertebral angiography, (B) carotid angiography and phlebography; II. Encephalography; III. Laminagraphy; IV. Myelography; and V. Varia.

The following are abstracts of papers read at this Third Symposium.—*T. Leucutia, M.D.*

Decker, K. The displacement of the posterior cerebral artery in vertebral angiograms. *Acta radiol.*, Aug.–Sept., 1953, *40*, 91–95.

The authors attempted several methods of evaluating films of vertebral angiograms to determine whether or not posterior fossa tumors produced recognizable vascular changes consistently. They finally made a composite of all their known normals and established the limits of normal variation of the position of the posterior cerebral artery. With this as a standard they superimposed the films of 26 known tumors and found that the posterior cerebral artery ran outside the normal limits in 20 per cent of the cases. This deviation was distinct enough to establish the diagnosis of a mass in the posterior fossa. These 20 per cent were operated on without further study.

Use of this method and further study should make vertebral angiography a more valuable procedure.—*F. M. Windrow, M.D.*

Olsson, Olle. Vertebral angiography. *Acta radiol.*, Aug.–Sept., 1953, *40*, 103–107.

The study of the intracranial distribution of the branches of the vertebral artery can be accomplished effectively and safely by catheterization of the radial artery. A ureteral catheter is inserted through an incision in the forearm and manipulated upwards into the vertebral artery.

The procedure was attempted in 240 cases, failed in 1 case, was incomplete in 1 case, failed on 1 side but was successful on the other in 5 cases, and was accomplished successfully without difficulty in the remainder.

The complication which caused occasional difficulty was arteriospasm. By premedicating the patient with 2 cg. papaverine sulfas intramuscularly this has been practically eliminated. There were no instances of perforation of a vessel or disturbance in the blood supply as a result of ligation of the radial artery.

The method was of very definite diagnostic value in the vascular cases, as was anticipated. This was the group in which study of the vessels was indicated for demonstration of arterial aneurysms or arteriovenous aneurysms. It was also useful in the posterior part of the brain in the same way as carotid angiography is valuable in the anterior part. Particularly was this true in central basal lesions such as pineaoma. It was diagnostic in 6 of 7 cases of hemangioblastoma of the cerebellum. In 14 patients with acoustic neurinomas there were 9 cases showing vessels directly related to the tumor and in 5 cases there were no such vessels, but there was displacement of the basilar artery and superior cerebellar artery.

In the cerebellar medulloblastomas the method, to date, has been somewhat disappointing. The vertebral system does not bear a regular relationship to the midline as does the carotid system, and its branches are more variable. Therefore, displacements are much more difficult to recognize. However, further experience and knowledge of the anatomy may increase the usefulness of the method in the cerebellar gliomas.—*Lois Cowan Collins, M.D.*

Sjögren, S. E. Percutaneous vertebral angiography; a review of 250 cases. *Acta radiol.*, Aug.–Sept., 1953, *40*, 113–127.

Modification in the technique of percutaneous puncture of the vertebral artery described by Lindgren in 1950 has reduced the hazards of the procedure, and, using 35 per cent diodrast (umbradil), complications have been minimal.

The examiner presses two fingers of the left hand between the vessels and trachea, and introduces the needle near the midline, directing it upward and outward so that it passes along the under surface of the transverse process.

In more than 150 cases examined by the method it was possible to perform percutaneous vertebral

angiography in all but 2 cases. These 2 patients were restless, and no attempt to do the procedure under general anesthesia was made.

The precutaneous method seems to have several advantages over the catheter method:

1. It does not necessitate ligation of an artery (the radial artery is ligated in the catheter method).
2. It can be accomplished with the same equipment as carotid angiography.
3. The choice of side is not limited.
4. There is not the hazard of perforation or injury of the vessels which exists with the catheter method.

The results have been very satisfactory. In 38 confirmed cases of posterior fossa expanding lesions, the presence of the lesion was demonstrated in all but one. In a few cases localization was not as precise as by pneumography.

Vertebral angiography is done in all cases of subarachnoid hemorrhage in which arteriovenous malformation has been found on carotid angiography (to demonstrate whether there are branches into the malformation from the vertebral artery), and in all cases of subarachnoid hemorrhage in which carotid angiography is negative.—*Lois Cowan Collins, M.D.*

FISCHGOLD, H., DAVID, M., TALAIRACH, J., and BREGEAT, P. Direct opacifying injections into the venous system of the head. *Acta radiol.*, Aug.–Sept., 1953, *40*, 128–138.

The authors review and discuss the methods of opacification of the veins of the head. Indirect opacification may be performed by means of carotid or vertebral angiography.

At St. Anne Hospital a simple film changer is used, allowing six exposures in six to eight seconds. The cerebral veins are visualized on the last three films. However, the diploic veins, the veins of the scalp, the pterygoid and occipital plexuses, tributaries of the external and posterior jugular veins cannot be demonstrated normally.

Direct injection into this venous system, therefore, becomes necessary. This may be accomplished by direct sinusography. The injection may be made, without high pressure, into the superior sagittal sinus, or with high pressure against the blood stream into the anterior part of the superior sagittal sinus above the foramen cecum, or at the cornonal suture. In the latter, opacification of the falx cerebri and tentorium has occurred. This, obviously, indicates the presence of a venous system in this area, which is unrecognized by anatomists.

Epileptic fits have been observed after extravasation of the contrast medium into the subarachnoid space due to rupture of a vein (the medium was completely absorbed in thirty minutes). One death was reported. The authors feel that, until a safe and nonirritating contrast medium is available, the examination should not be attempted.

Diploegraphy is performed by injection, with or without high pressure, into the occipital protuberance. If the diploic structure is thick, the trocar may be inserted in other parts of the skull.

By diploegraphy it is possible to demonstrate the external and posterior jugular veins and the anastomosis between the venous circulation of the brain, the meninges, the great sinuses, the vault, and the arachnoidal plexuses.

Reproduction of excellent roentgenograms accompany the article.—*William H. Shehadi, M.D.*

GVOZDANOVIĆ, V., and RIESSNER, D. Angiographic studies in the problem of brain revascularization. *Acta radiol.*, Aug.–Sept., 1953, *40*, 139–154.

The normal venous drainage of the brain was investigated by cerebral arteriography and retrograde venography in 16 patients. In order to attempt revascularization of the brain in patients with mental retardation and epilepsy, the Beck operation was then performed on 12 patients by ligating proximally the internal jugular vein on the side on which the transverse sinus was better developed, ligating all branches of the vein to the base of the skull, and creating a carotid-jugular anastomosis.

Injection of contrast material into the common carotid artery below the fistula after the Beck operation showed that all of the contrast material which passed through the fistula then passed to the venous communications within the skull and directly out of the cranium without ever filling the superior sagittal sinus, the straight sinus, or the superficial veins of the cerebrum. In no case did the internal jugular vein fill better after production of the fistula than with retrograde injection of the vein preoperatively.

None of the patients improved clinically, and one required closure of the fistula due to increased epileptic fits, headache, apathy, and unbearable cerebral pulsations.

The authors conclude that the circulation to the brain is not only unimproved by the fistula, but also a substantial portion of the arterial blood is shunted to the descending veins of the neck, reducing arterial flow to the brain and possibly overburdening the right side of the heart.—*Fay H. Squire, M.D.*

JOHANSON, CURT. The cerebral phlebogram by carotid angiography in cases of central brain tumours. *Acta radiol.*, Aug.–Sept., 1953, *40*, 155–172.

In the angiographic literature interest has been focused on the displacement of arteries, and little attention has been given to the position and appearance of the central veins. An expanding lesion may influence either the arterial or venous system or both.

In this paper only central and centrally infiltrating processes are discussed. The anatomy of the central veins was studied in cadavers by injecting barium sulfate in gelatine through the straight sinus. Films were exposed in different projections and then the results checked by dissection. These examinations were compared with 200 normal angiographies (of patients in whom the history, clinical symptoms, and course of the case and encephalography excluded expanding or atrophic processes).

From these studies the courses and variations of the deep cerebral veins are described and illustrated by roentgenograms and diagrams. Displacement of these veins may be recognized with sufficient accuracy to be diagnostic of an expanding lesion.

Eleven cases, all confirmed by operation, autopsy, or pneumography, are described and illustrated. The type of displacement varies according to the location of the tumor. Tumors originating in the basal ganglia straighten and depress the basal vein and displace it medially. A tumor in the posterior part of the corpus callosum straightens the middle and posterior part of the internal cerebral vein and displaces it basally. Tumors in the anterior part of the corpus callosum compress the anterior part of the internal cerebral vein from in front. Pineal tumors straighten the posterior part of the internal cerebral vein and may displace it laterally.

For accurate localization of these veins it is essential to have roentgenograms taken at right angles, *i.e.*, both anteroposterior and lateral views.—*Lois Cowan Collins, M.D.*

Löfgren, F. Olov. Carotid angiography in the diagnosis of spontaneous intracerebral haemorrhage. *Acta radiol.*, Aug.–Sept., 1953, *40*, 173–181.

The author presents 6 cases of intracranial hemorrhage out of 54 he had investigated by angiography between 1947 and 1951. All were examined within six weeks of their bleeding.

He divides the 54 cases into 5 groups:

1. Angiograms show an expansive process in the subcortical gray matter, *i.e.*, not encroaching on central structures. These cases are accessible to surgery.

2. Expansile process involves deeper structures (basal ganglia)—not amenable to surgery.

3. Normal angiogram—small hemorrhage or small areas of softening. Not operable.

4. Thrombosis of an artery. Not treated surgically.

5. Aneurysms—accessible to surgery.

Twelve of his cases were in Group 1, and all recovered. Ten of them were treated surgically.

Seven cases were in Group 2. Two of these were treated surgically. All cases died.

The author employed the same type of contrast medium used in this country (umbradil 35 per cent). He had only 2 out of all his cases in which he thought there might be a complication resulting from the angiography. Both developed a hemiplegia which gradually subsided. He advocates angiography in the acute stage for as early a diagnosis as possible. Angiography can, he states, differentiate thrombosis from hemorrhage and also the subcortical lesions can be differentiated from those involving the basilar ganglia.—*F. M. Windrow, M.D.*,

Richter, Hs. R. Phlebography in brainstem tumours. *Acta radiol.*, Aug.–Sept., 1953, *40*, 182–187.

The author has used the anterior and posterior choroidal and posterior choroidal arteries which anastomose in the region of the choroid plexus in the temporal horn and thus more or less surround the thalamus as guide marks for brain stem tumors. These vessels are easily displaced. The value of using these vessels is diminished by the fact that they cannot be regularly visualized by either carotid or vertebral artery injection.

He points out that the basilar veins drain from the choroid plexus of each temporal horn into the ampulla of Galen and thus furnish a more reliable landmark than the choroidal arteries.

He has also noted displacement and distortion of the internal cerebral vein which lies just above the third ventricle and pineal body, and also the striothalamic vein which drains the choroid of the lateral ventricles as a movable landmark for localizing deep-seated tumors.

Good diagrams of these venous channels are included in the article. One case illustrating the use of the above veins in localizing a brain stem tumor is offered.—*F. M. Windrow, M.D.*

Childe, Arthur E., Parkinson, Dwight, and Hoogstraten, Jan. Ventriculographic examination of the aqueduct of Sylvius and fourth ventricle; a report of five unusual cases. *Acta radiol.*, Aug.–Sept., 1953, *40*, 211–219.

Accurate ventriculographic localization of lesions deforming, displacing, or obstructing the sylvian aqueduct and fourth ventricle can be made if a sufficient amount of gas is used.

Oxygen is preferred by the authors who feel that the use of relatively large quantities is justified by the increased accuracy of diagnosis.

Ventriculography is performed in the morning and, if the findings indicate the necessity of operative intervention, craniotomy is performed as soon as possible during the same day.

The routine study calls for stereoscopic anteroposterior and lateral "brow-up" roentgenograms made with the patient in the supine position. The films are developed immediately and inspected. If the lateral ventricles are enlarged with no gas in

the third ventricle, further attempts are made to fill the latter. If a dilated third ventricle is demonstrated, it is assumed that there is an obstruction beyond that level. The patient is then turned to the prone position, the head lowered over the edge of the table and is shaken slightly to vigorously and in direct proportion to the degree of obstruction, to permit filling of the fourth ventricle. The patient is then placed again on the table, in the prone position, with a pillow under the chest, causing flexion of the neck. Three posteroanterior roentgenograms are made to provide two sets of stereoscopic films. This is accomplished by low centering of the roentgen tube for the first exposure with the central ray directed upwards to project the foramen magnum above the base of the skull, then moving the tube upwards the usual distance for a stereoscopic shift for two successive exposures. Additional right and left lateral sets of stereoscopic roentgenograms are also made.

The authors report 5 very interesting cases to illustrate some of the results of this ventriculographic procedure. In all but 1 case there was enlargement of the lateral and third ventricles, absence of or irregular filling or enlargement of the fourth ventricle, irregular or partial filling of the sylvian duct. Operative findings were as follows (Cases 2 and 3 died soon after operation, while the others are reported well):

Case 1: Five years old. Nodular tumors at the floor of the fourth ventricle. Histologically, these were glial tumors, consistent with tuberous sclerosis.

Case 2: Eleven years old. A cyst-like diverticulum of the right lateral ventricle (similar cysts were found in the spinal cord and right cerebellar hemisphere at postmortem).

Case 3: Twenty months old. An extensively growing astrocytoma was found.

Case 4: Forty-seven year old male. There was no dilatation of the ventricles. A 6 mm. displacement of the fourth ventricle to the right was present. There was a cerebellar tear with hemorrhage and blood clot following injury four days prior.

Case 5: Twenty-eight years old. A polypoid cystic tumor protruded through the foramen of Magenda. A companion cyst was also found. Histologically, these were identical with colloid cysts of the third ventricle.

Excellent reproductions of roentgenograms accompany these case reports.—*William H. Shehadi, M.D.*

FALK, BENGT. Encephalography in cases of intracranial tumour. *Acta radiol.*, Aug.–Sept., 1953, *40*, 220–233.

The author compares the relative merits of encephalography with air injected via the subarachnoid space by lumbar or cisternal puncture, and ventriculography performed by injection of air into the lateral ventricles through burr holes in the skull. He states that the literature is replete with statements and reports which are indefinite and contradictory as to the value of each procedure. The well known, immediate risks of ventricular puncture are damage to the brain tissue and intracranial bleeding.

The occurrence of calcification in the tract of the needles or beneath the burr holes in more than 10 per cent of cases is listed as a late complication. This complication would be completely avoided by encephalography. The two main objections to encephalography are (1) danger of foraminal herniation due to increased intracranial pressure, and (2) air may not enter the ventricles in certain cases with consequent inaccurate diagnosis.

The author feels that with proper technique, these objections may be obviated. He indicates that the patient should be in the sitting position, neck extended, head bent forward with chin back. He stresses the importance of injecting 5 to 10 cc. of air before removal of cerebrospinal fluid. Air rises rapidly and, in cases of increased intracranial pressure, will prevent herniation of the brain.

Films are exposed as the examination progresses, and if air is seen to enter the fourth ventricle and base of the aqueduct, then more air is injected.

The report is based on approximately 1,841 cases which were examined by this method and in 195 of which tumors were found. Good air filling, adequate for diagnostic purposes, was obtained in 95.1 per cent of the cases examined.

In encephalography, air on the convexities and in the basal cisterns is of particular value. In some cases, depending on the clinical history and findings, burr holes may be made first, and if encephalography does not bring about complete visualization of the ventricles, then ventriculography may be performed, thus combining the two procedures.

The combination of ventriculography or angiography for exact localization of tumor following diagnosis by encephalography was necessary in 14 cases and for verification of the diagnosis in 3 cases.

The author finds it more difficult to force air from the lateral ventricles through the foramen of Monro into the third ventricle, than in the opposite direction. Likewise, through encephalography, with the patients in the upright position, filling of the fourth ventricle and the aqueduct is more likely to occur than from above, following ventriculography. In reviewing the patients examined, the author presents cases illustrating this point and stresses its importance, particularly in suprasellar tumors, be they extra- or intracerebral, and in tumors in the region of the third and fourth ventricles and aqueduct.

The author concludes that the diagnostic results of encephalography are so excellent that they far outweigh the risks involved.—*William H. Shehadi, M.D.*

Ziedses des Plantes, B. G. Ventriculography with small amounts of air. *Acta radiol.*, Aug.–Sept., 1953, *40*, 261–266.

Ventriculography with small amounts of air may be applied to distribute a small amount of air over both inferior horns so as to depict them simultaneously. Ventriculography is a rather dangerous procedure, especially if an obstruction exists to the pathways of the cerebrospinal fluid. The risk may be reduced, first, by keeping the intracranial pressure at a constant level and, second, by introducing only small amounts of air.

In changes which give rise to obstruction of the third ventricle, the aqueduct of Sylvius, the fourth ventricle, or the basal cisternae or in those on the brain surface, ventriculography may be indicated. In such cases, ventriculography is a dangerous procedure if large quantities of air are used.

A small amount of air, *i.e.*, 10 ml. is injected into the lateral ventricles, in the newborn through the fontanel; in adult patients through burr holes. Some of the air may possibly pass into the descending horn. In order to get all the air into the anterior horn, the patient is placed in an upright position, with the head bent a little forward. Returning the patient to the supine position will cause all the air to enter the anterior horns. If the patient is turned over backward, the anterior part of the third ventricle will first of all be filled with air.

Making the patient turn a complete backward somersault causes the air to spread into the posterior part of the third ventricle and, if the aqueduct of Sylvius is not obstructed, into the fourth ventricle. If there is no obstruction, the air will escape to the cisterna magna and occasionally to the spinal canal.

It is also possible to obtain a representation of the fourth ventricle in cases in which no obstruction is present, if the backward somersault is completed quickly. If the procedure is performed slowly, the air will escape into the spinal canal.

The Forward Somersault: If the air escapes into the spinal canal, it may be brought into the basal cisternae by turning the patient again. If no obstruction is noted, the air will cross the basal cisternae to the surface of the cerebral hemispheres. If the air lies in the spinal canal, it may be necessary to bring the patient into a more upright position.

After having collected all the air in one of the anterior horns, the head of the patient is brought into an overhanging position in order to distribute the air into both anterior horns.

The patient is now returned first to the upright and then to the prone position. Following this, if the patient is made to perform the forward somersault, all the air will be distributed over both inferior horns.

The third and fourth ventricles, as well as the basal cisternae and the brain surface, may be examined by means of small quantities of air, by making the patient turn a complete backward somersault followed by a forward somersault, or at least by making the head of the patient describe such movements.—*Stephen N. Tager, M.D.*

Bourdon, R. Cranial tomography in neuroradiology. Tomography of the base of the skull. *Acta radiol.*, Aug.–Sept., 1953, *40*, 272–279.

The technical and practical applications of laminagraphy of the base of the skull are discussed. No illustrations are included because of the poor reproduction of this type of film. The tube and film were moved through an angle of 50 to 60 degrees. The optimum thickness was 5 mm. with a focus distance of 1 meter.

Orbital tumors were investigated, primarily those cases presenting as unilateral exophthalmos. Sagittal or frontal sections outline the internal orbital wall, lesser wing, anterior clinoid, cribiform plate, lateral wall of the sphenoid sinus, optic foramen, and orbital groove. The inferior orbital fissure is seen only in the submento-vertical projection. Changes in these structures were seen in optical, olfactory or sphenoidal lesser wing meningioma, ethmoido-fronto mucocele and carotid aneurysm. These produced weak points in the orbital walls, reactions in the ethmoidonasal sinuses, increase in size of the orbit, and adjoining structural alterations.

The olfactory fossa was investigated in the frontal and sagittal planes to show particularly the cristagalli as well as the cribiform plates, nasal fossae, and clinoids. When calcifications or hyperostosis are seen on plain films in the region of the sphenoid ridge the extent of meningiomas may be determined by displacement of the cristagalli, widening of the olfactory fossa, bulging of the cribiform plate, and distortion of the ethmoid cells.

Laminagraphy of the region of the sella outlines the anterior clinoid processes and thus distinguishes signs of global hypertension from local lesions arising in the region of the clinoids. Erosion, thinning, symmetry, displacement, and the distance between the anterior clinoids can be determined in cases of meningioma, chiasmal glioma, or internal carotid aneurysm. The sella itself was examined by means of frontal laminagraphy to show the effects of pituitary tumors. The various points noted were the height of the floor of the sella, the interclinoid distance, and the continuity of the level between the superior margin of the petrous pyramid and the superior margin of the floor of the sella.

The temporo-sphenoidal fossa showed a shrinking with cerebral atrophy or a deepening and parietal thinning in hydrocephalus.

The petrous bone was difficult to interpret because of its anatomic complexity and uneven density. It was examined only when indicated by anbormalities seen in ordinary films of this area.

Laminagraphy of the posterior fossa was valuable in congenital deformities of the skull and cervical spine and basilar impression.

Spheno-occipital junction tumors (chordoma and chondroma) are well outlined in the sagittal projection.—*Fay H. Squire, M.D.*

Odén, Sven. Diagnosis of spinal tumours by means of gas myelography. *Acta radiol.*, Aug.–Sept., 1953, *40*, 301–313.

Myelography may be carried out with positive or negative contrast media.

The disadvantages in the use of iodized oils are discussed in detail.

The advantages of using gas are numerous. The method is not dangerous. Hypersensitivity to gas is nonexistent. No toxic after-effects upon the membranes, in the form of arachnitis with residual adhesions and granuloma formation, have been observed. The gas is absorbed and leaves no traces. Examinations may thus be repeated if necessary. Myelography may be performed upon less restricted indications than with a positive contrast medium. Fluoroscopy is unnecessary.

The disadvantage of the method is that it is more time-consuming than the iodized oil method. With older patients, the indications for gas myelography should be more limited. A greater need for technically good roentgenograms is imperative. Subjective symptoms, such as headache and nausea, on the other hand, are somewhat more pronounced with gas.

The technique is described in detail.

Laminagraphy is used regularly in the investigation of the thoracocervical junction, since the bones of the shoulders and the thick musculature usually complicate the production of a technically good conventional roentgenogram. Laminagraphy is also employed on the parts where a change is suspected. It cannot be routinely used on the entire vertebral canal as the radiation dose would be excessive.

If the clinical examinations, such as double puncture and Queckenstedt's test, have given clear indications of a complete block in the subarachnoidal space, it is possible to spare older patients considerable discomfort by using only a small quantity of gas (20 to 30 cc.) injected by lumbar puncture to localize the lower limit of the obstruction.

Since 1938 more than 2,100 gas myelographies have been performed at Serafimerlasarettet, Stockholm, Sweden. The results, taken from a five year period, from 1947 to 1951, are presented.

The material obtained comprises 115 cases, all verified by operation or autopsy. The changes in these cases, in relation to the membrane of the vertebral canal, were situated as follows: intramedullary 24, extramedullary 88. Of the latter 59 were intradural (juxtamedullary) and 29 were extradural. In addition, the material includes 1 meningocele and 2 cases of kyphotic myelopathy. The youngest patient examined was a seven year old boy with an astrocytoma; the oldest, an eighty year old woman with a meningioma.

It was possible to establish an exact level of the lesion in 109 of the 115 cases, that is to say in 94.8 per cent. The roentgenologic and operative findings did not agree in 6 cases.

Of the 6 incorrect diagnoses, 4 may be attributed to the human factor. In the first case a meningioma at the level of the 7th thoracic vertebra had been overlooked. In the second, an extradural malignant tumor on the posterior side of the dura at the level of the 5th, 6th and 7th thoracic vertebrae was missed. In the third, a herniated disc between the 7th and 8th thoracic vertebrae was found at operation. In the fourth case the results of the roentgenologic examination were partially correct. A relative obstruction of the passage was observed at the level of the inferior border of the 12th thoracic vertebra. At operation the dural sac was found to be blocked at that site by arachnoid adhesions. However, laminectomy on the 6th and 7th cervical vertebrae was also performed, and revealed the presence of numerous small tumors originating from both the posterior and anterior roots on both sides. It was a typical picture of multiple neurofibromas.

Of the 2 remaining cases, those which could not be attributed to the human factor, 1 exhibited a syringomyelitic cavity at the level of the 5th, 6th and 7th cervical vertebrae at operation. In the sixth and final case, an intramedullary tumor, smaller than a hazelnut, was found at the level of the 8th thoracic vertebra, causing only a very slight expansion of the medulla. No changes were observed at the roentgenologic examination, nor were any found on later study of the roentgenograms.

The majority of the errors in these 6 cases depended upon the examiner.

The pathologic changes in 3 cases were localized to the middle part of the thoracic vertebral canal and in 1 case to the lowest part of the cervical canal. With regard to the type of the changes, in 3 cases they were extradural and in 1 case juxtamedullary, indicating that small extradural lesions are easier to overlook.

It appears that gas myelography is just as dependable as lipiodol in the diagnosis of expanding lesions in the spinal canal.

A recapitulation of all materials shows that myelography, regardless of the method, has a reliability of approximately 95 per cent.

The more detailed localization of tumors, as intra- or extramedullary is somewhat more difficult with gas than with positive contrast media. Such localization could be made definitely in only 30 cases; these were principally of the intradural juxtamedullary type.—*Stephen N. Tager, M.D.*

McRae, D. L. Bony abnormalities in the region of the foramen magnum: correlation of the anatomic and neurologic findings. *Acta radiol.*, Aug.–Sept., 1953, *40*, 335–354.

Over 100 patents with bony abnormalities in the region of the foramen magnum were available for analysis. The anatomic findings were correlated with the symptoms and clinical signs. Four groups for discussion were selected. (a) Occipitalization of the atlas, 28 cases. (b) Pure platybasia and basilar invagination, 21 cases. (c) Separate odontoid process of the axis, 11 cases. (d) Chronic atlanto-axial dislocation, 6 cases. The remaining cases formed a miscellaneous group, impossible to analyze.

Occipitalization of the Atlas. The essential point in the diagnosis is some degree of bony union between the skull and the atlas. The parts of the atlas to be clearly visualized are the anterior and posterior arches, the superior facets, and the transverse processes. Any or all of these may be fused with the skull.

It is important to realize that platybasia and basilar invagination are uncommon in association with assimilation of the atlas. Even when present they are slight and unimportant.

The most significant findings were related to the odontoid process of the axis. If the odontoid process was excessively long or unusually high in position, or if it was angulated posteriorly, symptoms and clinical signs were usually found.

Gas myelography was valuable in showing herniation of the cerebellar tonsils, the Arnold-Chiari malformation, and the presence or absence of a dural band pressing against the back of the cord at the level of the foramen magnum.

Neurologic symptoms and signs often appeared after a head or neck injury, and yet in none of these patients was a fracture shown.

Basilar invagination or impression means an upward bulging of the margins of the foramen magnum. It may be a congenital abnormality or secondary to softening of the bone about the foramen magnum. If the tips of the condyles are seen at or above the foramen magnum line, basilar invagination must be present. The tip of the odontoid process of the axis is above Chamberlain's line in about one-third of normal individuals. If the tip is more than 3 mm. above Chamberlain's line, basilar invagination is almost surely present.

Eight patients had no symptoms or clinical signs that could be caused by the foramen magnum lesion. Ten cases had symptoms and clinical signs that were considered to be due to the lesion.

A common finding was a convex clivus. It was found in 12 patients in contrast to only 4 patients in the group with assimilation of the atlas.

Of the 11 examples of *separate odontoid process*, 2 were certainly congenital abnormalities. Both were found accidentally, 1 in a nine year old boy who had had a head injury and the other in a seven year old epileptic. In both cases the odontoid process was fused to the anterior lip of the foramen magnum but did not encroach on it. It is not possible to decide in adults whether on old ununited fracture of the odontoid process or an anomaly is present.

In none of the group was platybasia noted. Only 2 showed basilar invagination. In both cases it was minimal. A striking finding was the marked gliding of the atlas on the axis during flexion and extension of the neck. This varied from 5 to 25 mm. and averaged 14 mm. in the symptomatic cases and 10 mm. in the asymptomatic cases. In all cases the separate odontoid process moved with the anterior arch of the atlas. The head flexed and extended at the atlanto-axial joint instead of at the atlanto-occipital joint. In none was evidence of bony fusion present between the atlas and the skull.

Eight of the 11 cases showed neurologic symptoms and signs. In 3 cases the patient had been referred with a provisional diagnosis of multiple sclerosis and in 1, syringomyelia.

Chronic Atlanto-axial Dislocation. One of the best examples was almost certainly a congenital abnormality. Two other cases had cervical block vertebra, 1 at C_2—C_3 and the other at C_6—C_7, suggesting the possibility of a congenital basis. The odontoid process was not particularly abnormal in shape.

One-third to one-half of the cases in each group are asymptomatic. Other cases have variable symptoms and signs suggestive of multiple sclerosis, syringomyelia and syringobulbia, or even brain tumor.

The author suggests that all cases of syringomyelia and syringobulbia as well as those suspected of having multiple sclerosis be referred to the radiologist for examination of the region of the foramen magnum. Certain cases have improved after surgical treatment of the above-mentioned conditions. Others have had no progression of symptoms or signs after operation.—*Stephen N. Tager, M.D.*

Sjögren, S. E. Experiences in localisation of brain tumours by means of diiodo^{131} fluorescein. *Acta radiol.*, Aug.–Sept., 1953, *40*, 356–360.

Two lead-shielded mica window Geiger tubes, connected to two scalers operating synchronously were used to investigate the uptake of diiodo^{131} fluorescein in the brain. A β particle absorption plate and a diaphragm were placed in front of the mica window. For correct positioning, areas to be measured were outlined on a rubber bathing cap worn by the patient.

A dose of 1.5 mc. was given. Thirty patients were examined. There was no difference in counting rate as a function of time in 3 meningiomas, 1 malignant glioma, and 1 normal case.

It was possible to localize, roughly, highly vascularized tumors, but not poorly vascularized processes. One tumor was localized to the opposite side. It was felt that the localization of tumors as well as the de-

termination of the nature of intracranial lesions was unsatisfactory for clinical use by this method, particularly since nothing was determined of the topography of the pathological process or the possibility of its removal. For these reasons pneumography and/or angiography are always to be preferred.—*Fay H. Squire, M.D.*

FISCHGOLD, H. Survey of the Symposium. *Acta radiol.*, Aug.–Sept., 1953, *40*, 369–370.

Dr. Fischgold, in concluding the Third Symposium Neuroradiologicum, gave a brief summary of the contributions which were made. The following facts have been demonstrated:

(1) In case of tumors of the vertebral canal, it is not enough to show only that a blocking of the spinal canal has occurred; inference may also be made as to the histology and the intradural or extradural location of the process.

(2) The importance of seriographic techniques may now be considered as well established. It will remain for the future, however, to determine which of the following three procedures will prove the most practical: (a) seriography on continuous or roll film; (b) seriography on cut film without cassettes; and (c) seriography on film in cassettes.

(3) In examining a frontal angiogram, careful study must be made to see whether there is any projection of the veins to the other side of the median line. This is a new sign of as much significance as the displacement of the anterior cerebral artery towards the healthy hemisphere.

(4) Vertebral angiography has been placed on a firmer basis and a pathognomonic sign has been established for the multiple tumors of Lindau.

(5) Encephalography is still used with considerable reserve in certain places and further verification is necessary.

(6) Laminagraphy, in which the author is particularly interested, seems to receive ever-increasing attention but this topic will be discussed in greater detail at the Fourth Symposium.

In closing, Dr. Fischgold paid high tribute to the Swedish neuroradiologists who made this excellent Symposium possible.—*T. Leucutia, M.D.*

ROWBOTHAM, G. F., HAY, RANKIN K., KIRBY, A. R., TOMLINSON, B. E., and BOUSFIELD, MARJORIE E. Technique and the dangers of cerebral angiography. *J. Neurosurg.*, Nov., 1953, *10*, 602–607.

During a twenty-three month period, cerebral angiograms were obtained in 450 patients. Three deaths, 12 severe and permanent complications and 18 transient complications occurred in the cases examined. In 14 there was dysphasia and in 10 there was mental confusion or some impairment of consciousness. Hemiplegia or some degree of limb paralysis occurred in every case.

The causes for the deaths and complications were investigated under three group headings: (1) the type of case selected for investigation; (2) the irritant nature of the contrast substance; and (3) avoidable or unavoidable faults in surgical techniques.

It was found that cases of cerebral thrombosis, acute and subacute head injury show a high incidence of complications. The method should only be used in cases of large cerebral tumors if the information will lead to better surgery. For the delineation of aneurysms, the method is essential if surgical treatment is planned. In degenerative encephalopathy the incidence is fairly high. It is felt that the method should be avoided in cases of doubtful clinical diagnosis, in the possibility that "something" might be found. Three different opaque media were used. None was found to be safer or to give better roentgenograms than the other.

In the 3 necroscopy cases there was hemorrhage in the periarterial tissues, but it was not felt that the bleeding had contributed to the death. There were intimal lacerations on the posterior wall of all the punctured carotid vessels up to 3 mm. in length.

In 2 selected cases bone flaps were raised and the cortex about the sylvian fissure was watched and photographed during the injection of the contrast substance and with normal saline. When injected rapidly and with force, dramatic color changes in the cerebral cortical background occurred. The cortex blushed again and returned to its normal color. This did not occur when the injection was performed slowly, either with the contrast substance or the saline. The impression obtained was that a column of fluid was driving a column of blood before it. If too much saline was used to keep the needle free of clot, the blood was washed out of the cerebral capillaries.

There did not seem to be any great relationship to the number of injections performed on each patient.

In order to minimize the complications, the authors advise the following:

(1) Careful selection of cases.

(2) Restriction of the number of roentgenological views, so that if lateral views give the required information no further films are exposed.

(3) The designing of a new syringe by which a minimal force of injection that gives adequate concentration of the contrast substance only is used.

(4) Discontinuance of the investigation when difficulty is experienced in entering the artery.

(5) The preparation of a more satisfactory form of opaque medium that can be injected slowly and produce an adequate concentration for roentgenography.

(6) The careful preparation of normal saline and use of a minimal quantity to keep the needle clear.—*Norman Heilbrun, M.D.*

RIISHEDE, JOHN and ETHELBERG, SVEN. Angiographic changes in sudden and severe herniation of brain stem through tentorial incisure;

report of five cases. *A.M.A. Arch. Neurol. & Psychiat.*, Sept., 1953, *70*, 399–409.

Failure of visualization of the cerebral arteries on angiography occurs in patients showing a sudden rise in supratentorial intracranial pressure with resultant herniation of the brain stem through the incisura tentorii but with no organic occlusion of the internal carotid artery.

Such a phenomenon was observed by the authors in 5 cases: the first showed a large cyst of the left cerebellar hemisphere causing obstruction of the fourth ventricle; the second showed a large glioblastoma involving the septum pellucidum, corpus callosum, and motor and premotor regions of both hemispheres, with obliteration of the foramina of Monro; the third showed hemorrhage originating in the right corpus striatum and filling the third ventricle and right lateral ventricle; the fourth showed a hemorrhage originating in the left basal ganglia and filling the left lateral ventricle and third and fourth ventricles; and the fifth showed a parasagittal meningioma involving both frontal lobes.

In all of these cases, organic obstruction as a cause of failure of visualization of the internal carotid system was excluded by postmortem examination. Temporary obliteration due to compression or spasm of the internal carotid artery is theoretically possible. However, increase in the intracranial pressure sufficient to cause compression of the internal carotid artery against the base of the skull should also cause compression of the basilar artery, and complete cessation of cerebral circulation would be fatal in the space of a few minutes. Spasm sufficiently severe to cause obliteration of an artery as large as the internal carotid is a remote possibility and the fact that in all cases the external carotid artery and its branches were well visualized and showed no evidence of spasm argues against such an occurrence.

The most likely explanation, therefore, for the failure of visualization of the internal carotid artery in these cases lies in the interrelationships of intracranial and intravascular pressures. It has been demonstrated that it is possible for intracranial pressure to exceed the pressure in the internal carotid artery and it has also been demonstrated that pressure on the brain stem can cause a reflex fall in cardiac output. It seems likely, therefore, that a diminution in cerebral blood flow due to these factors is the reason for the failure of visualization of the internal carotid artery and its branches.—*Leslie K. Sycamore, M.D.*

Petit-Dutaillis, D., Pertuiset, B., Rougerie, J., and Namin, P. Indications et résultats de l'angiographie vertébrale en neuro-chirurgie. (Indications and results of vertebral angiography in neurosurgery.) *Presse méd.*, Nov. 18, 1953, *61*, 1499–1503.

In 162 vertebral arteriograms there were 4 serious complications, 2 of them fatal. One fatality followed intra-arterial injection of 5 cc. of 1 per cent novocaine; another arteriosclerotic patient died three days after arteriography, the postmortem examination showing only calcification of the mitral valve and an old area of softening in the left cuneus. The role of arteriography per se is not completely clear in this case. One patient suffered a left hemianopsia, followed by left hemiparesis, both of which cleared up. The fourth complication was that of hemiparesis, which also cleared up. Contraindications to vertebral angiography include hypertension, renal insufficiency, severe arteriosclerosis, coronary insufficiency and iodine sensitivity.

The conditions studied were divided into four groups: (1) 45 vascular syndromes; (2) 44 subtentorial syndromes; (3) 16 diverse supratentorial syndromes; and (4) 43 diverse affections, such as epilepsy and hydrocephalus. Finally, in 13 patients the procedure was used to study the vascular supply of cirsoid aneurysms prior to carotid ligation.

In the vascular group there were, among 34 cases, 1 posterior cerebral arterial aneurysm, 2 cirsoid aneurysms of the cerebellum, 3 cirsoid aneurysms of the occipital lobe and 1 pinealoma. Other conditions found in this group included 3 calcified angiomas, 1 Sturge-Weber syndrome, 1 Knud-Krabbe disease, 1 diffuse familial calcification of Gehelin and Penfield, 6 cerebral arterites and 2 posterior cerebral thromboses.

In the subtentorial group of 44 patients there were 23 tumors.

In the supratentorial group of 16 patients there were 1 pituitary adenoma, 3 intracerebral hematomas, and 4 temporal lobe abscesses.

The arteriogram of cerebral arteritis presents enlarged, irregular, tortuous arteries with rigid segments and sharp angulations.

One meningioma and 1 pinealoma revealed tumoral vascularization; the other tumors caused only vascular displacement. Tumors of the cerebellopontine angle and deep, midline tumors may produce significant displacement. Posterior growth of pituitary adenomas may be delineated.—*Charles Nice, M.D.*

Poppel, Maxwell H., Jacobson, Harold G., Duff, Bedford K,. and Gottlieb, Charles. Basilar impression and platybasia in Paget's disease. *Radiology*, Oct., 1953, *61*, 639–644.

There is a fundamental and significant difference between basilar impression and platybasia. Basilar impression may be defined as an abnormal cephalad invagination of the foramen magnum region as determined by the relation of the odontoid process to Chamberlain's line. If the odontoid process is above Chamberlain's line, basilar impression is present. Platybasia is an abnormal obtuseness of the relation-

ship of two specific segments of the cranial floor. The first segment is represented by a line which extends from the nasion to the center of the sella turcica, and the second segment by a line extending from the latter point to the anterior margin of the foramen magnum. The inferior angle subtended by these two lines is termed the basal or sphenoid angle. The mean basal angle in normal cases was found to be 136.7°, with variations from 123° to 152°.

The authors did not find a significant incidence of platybasia in their series of Paget's disease of the skull; they found a definite trend (36 per cent of the cases) toward basilar impression. It is their opinion that routine evaluation of skull roentgenograms in all cases of Paget's disease is of more than academic interest. Mild, bizarre, unexplained symptoms and signs referable to varying degrees of cord compression may be explained by the demonstration of basilar impression.—*Arno W. Sommer, M.D.*

MORELLO, A. Pneumocisternography of the posterior fossa; preliminary report of a new technique. *J. Neurosurg.*, Sept., 1953, *10*, 552–554.

Visualization of the ventricular and cisternal cavities of the posterior fossa by injection of air into the lumbar subarachnoid space is described. The gas does not reach the intracranial cavity while it is being injected, but collects first in the lower part of the subarachnoid space and then ascends to the region of the foramen magnum in the quantity and with the speed and direction desired by the operator. "Control" of the air is obtained by tilting the table on which the patient is lying. The patient is placed on the side and a lumbar needle is inserted in the third and fourth lumbar interspace. Eight cubic centimeters of cerebrospinal fluid is withdrawn and 10 cc. of air is injected, and this is repeated until 30 cc. of fluid has been withdrawn and 40 cc. of air injected. The table is first tilted 5 degrees cephalically, the head-level being slightly, lower than the foot-level. The patient assumes a prone position and the head is placed with the canthomeatal plane perpendicular to the plane of the table. No motion of the head is permitted and a foot-rest prevents slipping downward. The table is now tilted 25 degrees cauadlly and three exposures in the lateral view at one minute intervals are made, centering through the mastoid. After an additional caudal tilt of 10 degrees (total 35 degrees), two more lateral exposures are made, with the head slightly and fully dorsiflexed. Finally the table is brought brought back to the horizontal position and two exposures in the postero-anterior view are made with the tube inclined 10 degrees and 30 degrees, centering 2 cm. below the external occipital protuberance. If visualization of the whole ventricular system is required, roentgenograms in routine views can be taken, as the amount of air is usually sufficient to give a good outline.

In cases of increased intracranial pressure, only 25 cc. of air is injected, 5 cc. at a time, a corresponding amount of cerebrospinal fluid being withdrawn.

The cisterna magna, the fourth ventricle, the aqueduct, and the posterior part of the third ventricle are usually visualized in the first three lateral views. The cisterna venae magnae Galeni is also frequently outlined as well as the vermis or at times the entire cerebellum. In the fourth and fifth lateral views, air is seen in the occipital horns and the pontine, interpeduncular and ambiens cisterns.

The advantages of this technique are: (1) the patient is horizontal during the exchange of the fluid-gas, and the procedure is therefore safer and less disturbing, particularly in cases of increased intracranial pressures; (2) no special equipment is needed; (3) the amount and movement of the gas are fully "controlled."

Four roentgenograms are reproduced showing the various areas as described.—*C. N. Borman, M.D.*

BROWNELL, GORDON L., and SWEET, WILLIAM H. Localization of brain tumors with positron emitters. *Nucleonics*, Nov., 1953, *11*, 40–45.

Tumor localization by coincidence counting of the annihilation radiation from positron emitting isotopes has the advantage of better resolution than can be obtained with single counters which are limited by scattering and colilmation. The physical principles of the method and the apparatus used are discussed; an example is illustrated but biological and clinical results will be presented elsewhere.

Theoretical considerations show that, in most materials, there is a 97 per cent probability that a positron will reach thermal energy and then be annihilated with the emission of 2 quanta in opposite directions with energies of 0.51 mev. This intraction occurs within 10^{-10} sec., and the range of the positrons is of the order of a few millimeters only so that essentially it may be regarded as occurring at the site of disintegration. Suitable isotopes with good positron emission, absence of gamma radiation, convenient half-life and suitable biological characteristics occur mainly in the middle atomic weight range and include V^{48}, Mn^{52}, Cu^{64}, As^{74}, Rb^{84}. (The work reported in this paper refers only to As^{74}.)

A pair of sodium iodide crystals and RCA 5819 photomultipliers mounted coaxially on each side of the patient's head from a carriage driven by a synchronous motor explore the required area in a series of horizontal strips 1 cm. apart, the coincidence and out-of-balance counts being recorded by followers which duplicate the movement of the detectors. A drawing, photograph and block diagram of the apparatus are included.

Calculations of sensitivity distributions transverse to and parallel with the detector axis are compared with measurements and with the corresponding single channel values. It is confirmed that scattering

and absorption, while decreasing the sensitivity do not alter the resolution. But with extended sources, the sensitive diameter is only about one-third of that for a single detector and as the spurious coincidences arising from the finite resolving time vary as the square of the activity, improvement in resolution is limited. Analysis of spurious coincidences shows that these cannot be removed entirely by reducing the resolving time because of counts due to simultaneous γ emission. Sharp discontinuities in activity superimposed on an extended background will be detectable. An example of the visualization of tumor location and extent is illustrated.—*R. S. Quick, B.S.*

Szlazak, J. Treacher Collins syndrome. *Canad. M.A.J.*, Sept., 1953, *69*, 274–276.

The Treacher Collins syndrome, first described in 1900, is a congenital deformity mainly of the face and occasionally of other parts of the body. The etiology is obscure. Mann mentioned that a disturbance of division and development of the mesodermal bone tissue during the fifth week of fetal life probably initiates this syndrome. Heredity may play an important role with transmission through the female line.

The syndrome is chiefly characterized by: (1) asymmetry of the skull with long occipitofrontal diameter and flattening of the occipitoparietal regions; (2) lack of marked nasofrontal angulation; (3) underdeveloped malars; (4) disproportionately large antra in relation to the small malar bones; (5) highly arched palate with malgrowing teeth; (6) hypoplastic mandible; and (7) absence or occlusion of the auditory meatus. Some cases show fused cervical vertebrae, abnormal costosternal structure and long metacarpal or metatarsal bones.

In cases where the signs of this syndrome are not pronounced, diagnostic roentgen examination is very helpful.—*William C. MacCarty, Jr. M.D.*

Neck and Chest

Gershon-Cohen, J., and Ingleby, Helen. Roentgenography of cysts of the breast. *Surg., Gynec. & Obst.*, Oct., 1953, *97*, 483–489.

This report is based on the study of cysts occurring in a series of 650 consecutive cases roentgenographed. Clinically the history of sudden onset of a large, freely movable, often tender and painful mass is in itself diagnostic of a cyst. A similar, although small mass in the opposite breast lends diagnostic confirmation. The sudden onset is stressed because certain other dysplasias, which are not sudden in onset, simulate cystic disease very closely. Thie distinction is important since some dysplasias do not need surgical interference whereas in others, operation is indicated.

Mazoplasia I corresponds with some restrictions to Geschickter's mastodynia and to desquamative epithelial hyperplasia of Cheatle and Cutler. Mazoplasia I is characterized by lumpy tender breasts, worse before menstrual periods. The lumps may come and go and the disorder may last for years. By palpation, it often requires a very experienced observer to distinguish a mazoplastic area due to intraductal fibrosis from a mass of cysts. It is here that roentgen examination can give its most efficient help, for cysts are absent on roentgenograms in both adenosis and mazoplasia I. Mazoplasia II is similar to mazoplasia I except for superadded simple cysts and adenosis. In both groups, there is a tendency to the formation of fibroadenomas. Most large simple cysts are found in mazoplastic breasts. In addition, one encounters occasional large apocrine cysts, large cysts of the secretory type and cysts with intracystic carcinoma (most often of the papillary type).

Noncystic conditions such as a fibroadenoma, abscess, adenosis and mazoplasia I may mimic a cyst very closely. A lump due to adenosis has a striking tendency to be large and very tender premenstrually and to regress almost completely after the menstrual period.

Cysts are rarely observed before the age of twenty-five and then they occur with increasing frequency until the forties. A cyst arising after the age of fifty-five should be regarded with suspicion.

Only cysts more than 0.5 cm. in diameter can be seen on the roentgenogram. They appear as well defined opacities with a smooth outline. Isolated simple cysts are usually spherical; conglomerate and loculated cysts are either oval or have irregularly scalloped borders. The normal fat component of breasts after the age of twenty-five aids in diagnosis since there is little difference in the density between cysts and breast parenchyma. The uniform density of a cyst helps to differentiate it from the trabecular structure of breast tissue. Bloody fluid or hemosiderin in cysts increases their density. Since a clear zone occurs about a cyst and also about a fibroadenoma and some carcinomas, this sign cannot be relied upon for determining diagnosis.

In the differential diagnosis, we must consider: (1) differentiation of cysts among themselves, and (b) differentiation of cysts from other breast lesions.

Simple cysts, the most common type, may be solitary, multiple, or conglomerate, and occurred in 47 per cent of cases verified by operation in this series. Apocrine cysts, while present in practically all women's breasts over thirty years of age, seldom attain clinical size and cannot be distinguished on the roentgenogram from simple cysts of the mazoplastic type.

Intracystic papillomas are much less common and, as a rule, cannot be differentiated from simple cysts, but on occasions may be suspected because of their remarkable visibility on the film and due to increased vascularity of the adjacent breast.

In differentiation of cysts from other breast lesions, the fibroadenomas may simulate them so closely as to be indistinguishable. A conglomeration of cysts may suggest the bosselations of a fibroadenoma.

When calcification is present, it is usually disseminated through the substance of a fibroadenoma, but only in the capsule of a cyst. Mazoplasia I or mastodynia, while confused clinically with a cystic condition, can be ruled out by the roentgen examination since cysts are absent.

Chronic abscess should be suspected when the lesion shows indistinct margins, swollen perifocal trabeculae and considerable increase in vascularity of the surrounding tissue. These signs are also suspicious of a carcinoma. In malignant lesions there may be a comet-like tail extending out into the surrounding structures. This tail, of course, must be continuous with the tumor and not due to superimposed structure. When calcifications are present, they are dispersed widely in and around malignant lesions and not in plaque-like deposits as in cyst walls.—*Robert K. Arbuckle, M.D.*

HOCHBERG, LEW A. Primary tumors of the rib; review of the literature and presentation of eleven cases not reported previously. *A.M.A. Arch. Surg.*, Oct., 1953, *67*, 566–594.

The author presents the salient findings in primary tumors of the rib from a review of 205 cases collected from the literature, adding 11 cases of his own; 52 per cent were benign, 48 per cent malignant.

Among benign primary tumors were, in order of frequency, fibrous dysplasia, chondroma, osteochondroma, xanthomatous giant cell tumor, hemangioma, osteoma, and others. The malignant primary tumors included chondrosarcoma, Ewing's endothelioma, fibrosarcoma, mixed sarcoma, osteogenic sarcoma and others.

Pain and swelling are the most frequent symptoms of both benign and malignant primary rib tumors. Endotheliomas, sarcomas and lymphosarcomas occur more commonly in patients under 30 years of age. A tumor confined to a single rib is more apt to be benign than malignant.

Chondromas usually appear as a local, well demarcated expansion of a rib with uniform density simulating a cystic area, in the anterior or cartilaginous part. Osteochondromas resemble chondromas, but in addition show mottled small areas of calcification within and along the periphery of the tumor. Lesions of fibrous dysplasia show an expanded thinned-out cortex, with the entire involved area translucent and irregularly traversed by denser bony trabeculae.

Chondrosarcomas appeared as fixed masses with areas of mixed bony and rarefied densities due to tumor degeneration. Osteogenic sarcomas resembled chondrosarcomas, but were denser and contained more areas of sclerosis. Fibrosarcomas also resembled chondrosarcomas, but were less apt to involve the anterior part of the rib. Of 12 cases, 9 involved portions of ribs proximal to the anterior axillary line. Endotheliomas produced variable roentgenographic appearances; sometimes resembling osteomyelitis, sometimes with only thickened cortex and sometimes having a laminated, "onion-peel," periosteal configuration.—*Walter T. Hileman, M.D.*

FRANCHINI, YAGO, and RIBÓ, JOSÉ. Los métodos de exploración del cavum nasofaríngeo en la infancia. (Methods of exploration of the nasopharyngeal cavity in infancy.) *Semana méd.*, Sept. 24, 1953, *103*, 446–453.

The methods of examination of the nasopharynx include rhinoscopy and nasopharyngoscopy, palpation, and roentgenography. Roentgenographic procedures include simple lateral roentgenograms, contrast roentgenography with lipiodol and laminagraphy. Enlarged adenoids causing hypoacusis, sinusitis causing nasal respiratory insufficiency, tumors, polyps, and abnormalities of the nasal bones may be depicted by these methods.—*Charles Nice, M.D.*

ELLMAN, PHILIP. Unusual manifestations of bronchial carcinoma. *Proc. Roy. Soc. Med.*, Oct., 1953, *46*, 851–858.

From his experience in a series of 200 consecutive cases of bronchial carcinoma the author discusses various manifestations.

The "silent" phase of the disease may be prolonged for months or years. Opaque rounded shadows discovered by routine mass roentgenography, particularly in males of the 40–60 age period, should be explored and radically resected if found to be malignant.

Acute or chronic polyarthritis may be the initial complaint in patients with carcinoma of the lung. Most of the patients in the author's series had been treated several months for rheumatoid disease. Arthralgias and arthritis in such patients are probably the earliest manifestation of hypertrophic pulmonary osteoarthropathy. In none of the cases was there any evidence of extensive tissue breakdown or appreciable infection in the lung so it was difficult to explain the association of the joint and lung conditions, yet removal of the lung carcinoma produced dramatic, sudden improvement of the joint lesions.

Bronchial carcinoma and pulmonary tuberculosis may co-exist. This is most common in males of the 50–60 age period. Differential diagnosis is notoriously difficult and exploratory thoracotomy should be encouraged in any doubtful case.

Certain pneumoconioses, such as those in Schneeberg miners and pulmonary asbestosis, have been incriminated as having a possible etiological relationship with bronchial carcinoma. Workers exposed to chromium compounds, nickel, arsenic and mica are also said to exhibit increased incidence of lung cancer.

Cases of carcinoma of the lung sometimes appear as general medical disorders. This series includes examples of lymphangitis carcinomatosa resulting in

"pyrexia of unknown origin" and "asthma," cases with low back pain with secondary deposits in the spine, cases of "virus pneumonia" and cases with cardiac manifestations such as auricular fibrillation and heart block.

It is concluded that the whole of general medicine can be involved in the diagnosis of atypical manifestations of bronchial carcinoma.—*Arthur E. Childe, M.D.*

Henson, R. A. Unusual manifestations of bronchial carcinoma. *Proc. Roy. Soc. Med.*, Oct., 1953, *46*, 859–861.

Carcinoma of the lung without associated relevant secondary deposits may be accompanied by various neurological syndromes. The author has seen 16 patients with carcinomatous neuropathy at the London Hospital, and in 15 the underlying carcinoma was found in the lung. The clinical manifestations of these neuropathies are varied and patients frequently show evidence of multiple lesions in the nervous system.

Subacute cerebellar degeneration presents a picture of rapidly progressive ataxia and dysarthria. Diplopia may be an early symptom, and euphoria and dementia are often present. Death usually occurs in a few months but 2 of the author's patients received early surgical treatment and survived for over two years.

Sensory neuropathy was present in 3 patients. They all suffered from paresthesias, pains in the limbs and ataxia. In only 1 of these patients were the neurological symptoms initial. Necropsy showed degeneration of the posterior root ganglia.

Two patients suffered from polyneuritis, and in each the motor and sensory changes in the limbs antedated the pulmonary symptoms by a few weeks.

Motor neuropathy and myopathy were found in 8 patients. The predominant clinical picture was that of a lower motor neurone lesion. Postmortem examination in 3 of them confirmed that this disorder was not due to secondary deposits.

The association between carcinoma of the lung and neuropathy is more than a chance one, and the occurrence of such syndromes should lead to an intensive search for carcinoma, especially in the lung. The available evidence suggests that the etiological relations of the neuropathy are with the carcinogen rather than with the carcinoma itself.—*Arthur E. Childe, M.D.*

Sellors, T. Holmes. Unusual manifestations of bronchial carcinoma. *Proc. Roy. Soc. Med.*, Oct., 1953, *46*, 861–863.

The author has analyzed the manifestations in 200 consecutive patients with carcinoma of the lung admitted to hospital. The main features were respiratory and only a small proportion could be referred to other systems. The term "unresolved pneumonia" should no longer be used since it has often been applied to growths beyond which there is infection and in which diagnosis has been unnecessarily delayed. Obstruction of a bronchus can give rise to a persistent wheeze which is sometimes only noted by the patient when he adopts a certain posture. No hemoptysis, however slight, can be ignored. Loss of voice due to involvement of the left vagus or recurrent laryngeal nerve may be the presenting symptom. A sudden onset of auricular fibrillation in a patient whose heart rhythm has previously been normal may indicate the spread of lung cancer along a pulmonary vein into the wall of the auricle. Metastases may occur in the suprarenal glands resulting in extreme weakness and pigmentation or even severe sudden collapse. Implantation in the small intestine occasionally results in intussusception.

Although patients with lung cancer are referred for treatment much earlier than they were ten years ago, the medical profession must still accept a great deal of responsibility for delayed diagnosis.—*Arthur E. Childe, M.D.*

Gibbon, John H., Jr., Allbritten, Frank F., Jr., Templeton, John Y., III, and Nealon, Thomas F., Jr. Cancer of the lung—an analysis of 532 consecutive cases. *Ann. Surg.*, Oct., 1953, *138*, 489–501.

In the period 1946 through 1952, 532 cases of primary carcinoma of the lung were seen at the Jefferson Medical College of Philadelphia and these form the basis of the present article.

There were the usual sex differences, age distribution and symptoms. Only 19 cases were asymptomatic.

In 85 per cent of the cases the roentgenologist made a correct presumptive diagnosis of bronchogenic carcinoma. Bronchoscopy resulted in biopsies in 25 per cent of those operated upon. Where bronchoscopic biopsy could not be obtained, cytologic studies of bronchial aspiration or washings gave the diagnosis in an additional 45 per cent of those operated upon. In almost one-third of the cases coming to surgery, the diagnosis was based purely on roentgen and clinical findings.

Surgical extirpation was largely limited to those patients in whom there was no evidence of spread outside of the operative field, palliative resection being avoided. The curative procedure attempted was pneumonectomy with removal of the regional lymphatics and occasional block resection of limited portions of the involved chest wall. Three hundred and eighty patients (71 per cent) were considered operable and were explored. In 205 (39 per cent of total) the lesion was removed. This high rate of exploration has resulted in a higher rate of extirpation and a higher rate of immediate salvage than other reported series of significant size. Of those who had their cancer removed, 45 (22 per cent) died before

leaving the hospital, and of those who had only an exploratory procedure, 20 (11 per cent) died. Thus, 30 per cent of the entire series left the hospital alive after apparently complete removal of the cancer.

Ipsilateral paralysis of the vocal cord was a poor prognostic sign. In every case (43) there were either distant metastases or the tumor could not be removed. Invasion of the chest wall also was a poor sign; 13 patients had resection of the chest wall and none survived as long as eighteen months.

Most of the cases had not been followed for five years, but of those which had been resected that long ago there was a 22 per cent survival (9 of 41 cases), or 9 per cent of the total seen. A curve including all patients indicates that most of the deaths in the extirpated cases in which there was no extension beyond the lung itself will occur within two years, after which the curve is almost flat.—*Henry J. Klos, M.D.*

BRAUN, H., and WEICKSEL, P. Zur röntgenologischen Differentialdiagnose multipler grobknotiger Lungenherde. (Roentgenologic differentiation of multiple, coarse densities in the lungs.) *Tuberkulosearzt*, Sept., 1953, *7*, 533–537.

Two cases are presented in detail having multiple coarse nodular densities disseminated throughout both lung fields. One case was found to be a confluent bronchopneumonia with multiple, small abscesses; the other, disseminated tuberculosis.

With a roentgen appearance as that in these 2 cases, one should also think of more rare conditions in addition to the more common explanation of metastases. If accompanied by a septic picture, embolic phenomena leading to focal pneumonias or abscesses must be suspected. The coarsely nodular type of hematogenous pulmonary tuberculosis is extremely rare. It is characterized by multiple, dense, usually sharply delineated nodules which may be as large as a chestnut. Extrapulmonary tuberculosis is usually present and helps in making the differential diagnosis. The sputum is usually positive. A similar appearance is present with the emphysematous form of miliary tuberculosis, except that the nodules here are less sharply delineated. Compression of small bronchioles by peribronchial foci and diminished elasticity of lung tissue produce the numerous small air saccules within the miliary foci.

Cysticercosis of the lung is another very rare condition presenting multiple coarse nodulation. The diagnosis is made by the specific reaction and the recovery of echinococcus cysts in the sputum.

Actinomycosis and the rare coarsely nodular type of pneumoconiosis are also mentioned.—*Frederick M. Reis, M.D.*

WOLF, BERNARD S., SOM, MAX, and MARSHAK, RICHARD H. Short esophagus with esophagogastric or marginal ulceration. *Radiology*, Oct., 1953, *61*, 473–495.

Twenty-nine cases of short esophagus with peptic ulceration at the esophagogastric junction are reported. Emphasis is placed on the roentgenologic and esophagoscopic findings. The authors state that they chose the term short esophagus because the roentgen findings indicated that the esophagus was not redundant and emptied into the top of a gastric pouch above the diaphragm. The esophagoscopic findings show a distance of from 25 to 37 cm. from the incisor teeth to gastric epithelium, while normally the distance is from 38 to 40 cm. Whether the short esophagus was congenital or acquired is a matter of conjecture.

Outstanding features, in addition to the above, were free reflux from the gastric herniation into the esophagus in spite of the relative narrowness of the junction and the constant esophagoscopic findings of ulceration. The ulceration was usually superficial and a crater could be demonstrated roentgenologically in only 6 of the 29 cases. All the patients were biopsied and the ulceration was at the esophagogastric junction with the proximal border of the ulcer showing esophageal mucosa while the distal portion showed gastric mucosa.

As a general rule, the 29 cases could be divided into those (22) in which some degree of stenosis was present and those (7) in which there was no narrowing demonstrable. In a few instances the findings could be obtained only after dilatation.

Frequently noted roentgen findings were a tent shape to the herniated stomach and a fusiform narrowing of the lower esophagus, both giving the appearance of traction applied from above and below the esophagogastric junction. In the common sliding type of diaphragmatic hernia the esophagus may or may not be short and the herniated portion of the stomach is rounded and bulbous.

In this group of cases, frequently noted symptoms were heart burn, bleeding, and severe pain which could be confused with coronary artery disease. There were no instances of perforation or association with other peptic ulceration. Treatment has been aimed at symptomatic relief and esophageal dilatation but the results have not been dramatic. —*Clyde A. Stevenson, M.D.*

NADAS, ALEXANDER S.; ROSENBAUM, HAROLD D.; WITTENBORG, MARTIN H.; and RUDOLPH, ABRAHAM M. Tetralogy of Fallot with unilateral pulmonary atresia; a clinically diagnosable and surgically significant variant. *Circulation*, Sept., 1953, *8*, 328–336.

The successful accomplishment of an aortopulmonary shunt in a patient with tetralogy of Fallot will depend to a large extent on the availability of a pulmonary artery through which systemic

blood can be directed to the lungs and on the presence of a second vessel to maintain pulmonary circulation during the period of temporary occlusion of the first pulmonary vessel. Accordingly the detection of cases of tetralogy of Fallot with unilateral pulmonary artery atresia becomes very important from the surgical standpoint. This variant of the tetralogy of Fallot is a well recognizable clinical entity and the present report considers 4 such cases. In 3 of these cases, in which the heart was in the normal position, there was atresia of the left pulmonary artery, while in 1 case with dextrocardia associated with tetralogy of Fallot, the atresia involved the right pulmonary artery. In all 4 cases, the uninvolved pulmonary artery was markedly dilated. All reported cases of atresia of one pulmonary artery without intrinsic heart disease have affected the right pulmonary artery.

Differentiation from the conventional type of tetralogy of Fallot is possible on the following grounds: (1) the systolic murmur (if present) transmits with maximal intensity in the right chest, not the left as in the classical type; (2) roentgen study shows marked diminution of pulmonary vascularity on the side of atresia with pulmonary engorgement and even a "hilar dance" on the side of the dilated artery; (3) angiocardiographic studies reveal an overriding aorta, atresia of one main pulmonary artery and aneurysmal dilatation of the other.

In one of the operated cases in this group, momentary compression of the right pulmonary artery resulted in a rapid and significant drop in arterial oxygen saturation. The hazard of temporary compression of the one pulmonary artery in the present type of case is too great to permit an attempt at establishing a shunt. The importance of the correct roentgenologic diagnosis is obvious.—*C. N. Borman, M.D.*

Locket, S. Calcification of the left auricle. *Med. Illustrated*, Oct., 1953, *7*, 763–767.

Four cases showing calcification of the wall of the left auricle during life are presented. Two of the cases are reported in detail. The other 2 were found on review of roentgenograms made in a series of 212 patients with mitral stenosis.

Possible mechanisms of calcification of the heart include: hypervitaminosis D, primary and secondary hyperparathyroidism, extensive bone destruction, chronic renal disease, localized rheumatic endocarditis, and calcification in degenerated myocardium.

The author believes that the calcification in 3 of his cases was due to calcific deposition in areas of localized rheumatic endocarditis, and in the fourth case to calcification in a degenerated auricular myocardium.

The only feature common to all the reported cases was the duration of underlying heart disease (14 to 54 years). Auricular fibrillation was present in all but one case.

This lesion should be differentiated from other heart conditions with calcification, such as myocardial infarction, calcification of coronary arteries, mural thrombi, calcification of ventricular and aortic aneurysms, calcification of mitral and aortic valves, and calcific pericarditis.—*D. V. Campbell, M.D.*

Abdomen

Russ, Frank H., Glenn, Donald L., and Gianturco, Cesare. Gas embolism during extraperitoneal insufflation; recovery in the left decubitus position. *Radiology*, Oct., 1953, *61*, 637–638.

Extraperitoneal air insufflation, done through a single presacral puncture, is a simple procedure which is considered safe by most workers. Gas embolism is not likely to occur because the needle inserted in the midline between the rectum and the sacrum encounters no large vascular channels.

The authors report a case of gas embolism during extraperitoneal insufflation. The slow administration of 500 cc. of oxygen, while the patient was on the left side, was well tolerated. The subsequent injection of 100 cc. of oxygen, with the patient in the prone position, brought on severe dyspnea and cyanosis. The pulse was rapid, irregular and threadlike and the blood pressure was very low. A loud "mill wheel" sound could be heard with each heart beat, indicating the presence of gas in the heart. Recovery followed return of the patient to the left-sided position.

The authors stress the fact that no insufflation is completely safe. Gas may enter the venous system even when the injection is done in tissues that are relatively avascular. In view of the evidence presented by the authors it seems that the serious effects of gas embolism may be avoided or minimized by using a slow rate of injection, by maintaining the gas at low pressure, and by keeping the patient in left decubitus during the injection and for some time thereafter.—*Arno W. Sommer, M.D.*

Harland, David. A case of multiple calculi in the large intestine with a review of the subject of intestinal calculi. *Brit. J. Surg.*, Sept., 1953, *41*, 209–211.

The author describes a patient in whom 166 primary calculi were found in the large intestine associated with megacolon and a stricture of the sigmoid colon at the site of a previous operation.

The subject of intestinal calculi is discussed. Primary calculi are those which have been found in the bowel, while the secondary ones have been formed elsewhere, in the biliary or renal tracts prior to becoming intestinal. Primary calculi may be either true or false; the former develop as a result of precipitation and deposition of substances found in the chymus under normal conditions, whereas the latter

are formed under special alimentary conditions such as the presence of undigestible material, the sedimentation of suspended insoluble salts, or inspissation of intestinal contents. Calculi composed of mineral salts such as magnesium phosphate, calcium phosphate, calcium carbonate and oxalate or bile acids comprise the majority of the primary true calculi. Bezoars, medicinal concretions, fecaliths and foreign bodies constitute the group of false calculi.

The factors concerned in the formation of stones are generally accepted as being chemical and mechanical. The chemical factors are due to an alteration in the local chemical conditions as may be caused by infection, altered metabolism, or a change in the hydrogen ion concentration. The mechanical factors are chiefly the result of conditions producing stasis, *i.e.*, obstruction and diverticula, and of the presence of preformed nuclei. Intestinal calculi usually contain food particles and dead and living bacteria.—*James F. Martin, M.D.*

FIGIEL, LEO S., and FIGIEL, STEVEN J. Volvulus of the cecum and ascending colon. *Radiology*, Oct., 1953, *61*, 496–515.

The authors report the roentgen findings in 24 patients with volvulus of the cecum, which are added to 447 previously available in the literature. The anatomical and clinical considerations are discussed.

Roentgenologically two main groups are identifiable. (a) In approximately 60 per cent of cases, due to completeness of obstruction, the distal colon is completely or relatively devoid of gas and fecal material. There is a tendency for the cecum to migrate to an abnormal location, the most common being the left upper quadrant. (b) The second group consists of cases of partial torsion, in which the incompleteness of the obstruction permits passage of gas into distal colonic segments, the degree of distention being such that the obstruction cannot be accurately localized without a contrast enema.

When the right colon is disproportionately distended one should suspect partial torsion of the right colon with incomplete obstruction. Suspicion of partial torsion may be enhanced by: (a) demonstration of a fluid level in the cecum; (b) demonstration of an apparent discontinuity of the gas pattern in the proximal colon near the hepatic flexure; (c) a progressive cecal distention on subsequent observations; (d) a progressive tendency toward cecal dislocation on progress studies; and (e) a characteristic obstruction on examination of the colon with a barium enema.

Fourteen descriptive figures of volvulus are included.—*Everett E. Seedorf, M.D.*

EKENGREN, KRISTINA, and SNELLMAN, BJÖRN. Roentgen appearances in mechanical rectal constipation. *Acta radiol.*, Nov., 1953, *40*, 447–456.

Patients complaining of constipation were studied by the authors. Two types of sensation experienced by the patient were frequently encountered. Type one was designated "pressure on the rectum from without," in which the patient described the sensation of a mass moving down and preventing the passage. Type two, "distention of the lower part of the rectum," was described as the feces collecting at the side of or in front of the anus so that manual pressure on the mass would facilitate the movement.

A technique was developed whereby roentgenograms were obtained in anteroposterior and lateral projections with the patient sitting on a stool that simulated a commode. The examination was carried out in three stages: (1) with contrast medium in the distal ileum, (2) with the rectum filled with semifluid barium and the vagina with highly viscous umbradil, and (3) after evacuation of as much barium as possible and refilling the vagina with contrast material. Roentgenograms were exposed with the patient relaxed and repeated with the patient straining.

In type one, cases of pressure from without, the authors demonstrated a mass in the rectogenital fossa compressing the anterior rectal wall. Compression occurred only when the patient strained. This mass was composed of a coil of small intestine, the sigmoid colon and the uterus. They believed the downward descent of the uterus to be the greater factor in producing the compression.

In type two, cases of distention of the lower part of the rectum, ballooning of the rectal wall either forward or laterally during the act of straining was demonstrated. Thus the rectal content remained pocketed and was not passed through the anal canal.

Cases which do not respond to medication, the authors believe, may be helped surgically, and the roentgenographic examination may indicate which operative method is likely to give the best results.—*Robert E. Flynn, M.D.*

ALEXANDER, FAY K. The prepyloric suspect lesion. *Radiology*, Oct., 1953, *61*, 523–533.

The responsibilities of the radiologist in reporting a gastrointestinal examination vary with the type of work the referring physician does. When a highly trained gastroenterologist receives a roentgen report of a suspicious lesion in the prepyloric area he understands the full implications of such a report but a general practitioner may not.

The author quotes the literature and presents several cases to show that the radiologist must convey his entire understanding of the prepyloric lesion to the general practitioner so that the most satisfactory treatment may be selected. No single finding or sign is reliable for differential diagnosis of gastric lesions and the radiologist must assume part of the responsibility for increasing the surgical exploration rate if gastric cancer is to be more successfully handled.—*Clyde A. Stevenson, M.D.*

Meschan, Isadore; Landsman, Harold; Regnier, George; Ward, H. Wendell; Broggdon, B. Gilliam; and Pool, Chalmers S. The "normal" radiographic adult stomach and duodenum; a study of their contour and size and their critical relationships to the spine in both symptomatic and asymptomatic individuals. *South. M. J.*, Sept., 1953, *46*, 878–887.

The authors studied 211 adult individuals, half being symptomatic and the other half asymptomatic, and made very accurate and comprehensive measurements of the size, contour, type, and location of the stomach and duodenum.

They divide the stomachs into four types, namely the J-shaped, the cascade, the fish-hook, and the steer-horn types. The individuals are classed on the basis of habitus as normal, underweight, and overweight.

The authors state that although the statistical number is small, their measurements indicate that, in general, the stomachs are larger in the asymptomatic than in the symptomatic patients. In the symptomatic individuals, there is a higher incidence of steer-horn and fish-hook type stomachs, especially in the normal and underweight groups. Statistically, it appears that when the steer-horn type stomach is encountered in anyone other than an overweight individual, it may be associated with symptoms. When the distance of the stomach from the spine is evaluated, the habitus of the individual must be considered.

There are, of course, wide variations in "normal" stomachs and it is recommended that when symptomatic individuals are examined, the roentgenological size, configuration, and position should be evaluated with respect to the "normal" individual of the same habitus. This contribution is unquestionably a step in the right direction. Further observations and measurements will increase its statistical value.—*C. L. Hinkel, M.D.*

Baker, Lester, and Gattas, Fred A. Primary benign peptic ulcers of greater curvature of stomach; review of the literature and report of four new cases. *A.M.A. Arch. Int. Med.*, Sept., 1953, *92*, 321–332.

The dictum that "all ulcers occurring on or closely adjacent to the greater curvature of the stomach are malignant until proved otherwise" has been accepted in the English literature almost unqualifiedly for the past two decades. Prior to the 1930s very few histologically proved benign greater curvature peptic ulcers had been described. The first published proved case, in 1914, was that of a peptic ulcer with chronic perforation into the spleen. Sporadic proved cases of benign ulcers on the greater curvature of the stomach appeared in the literature during the next twenty years. Mathews, in 1935, reviewed the literature and concluded that only 22 peptic ulcers of the greater curvature had been described in sufficient detail to warrant that diagnosis. Since 1935, 24 additional proved cases have been reported.

A review of the records from the Veterans' Administration Hospital, Hines, Illinois during the five year period from July, 1947 to June, 1952, revealed 4 cases with primary benign peptic ulcers on the greater curvature. During this period 305 patients with benign gastric ulcers were treated. In 119 of these histologic examinations of the stomach were made at either surgical or autopsy study.

The case histories of these 4 patients are given. All had proved benign ulcers on the greater curvature of the stomach. Three of the ulcers were near the pylorus and one at the junction of the middle and distal thirds on the greater curvature.

The incidence of benign ulcers occurring on the greater curvature is difficult to determine precisely. Various reports from different sources give percentage figures ranging from 0.7 to 14 per cent. If we accept the figure of 1 per cent from the cited statistics, as average for the occurrence of greater curvature benign ulcers, there still remains a gross discrepancy between this figure and the fewer than 40 documented cases reported in the literature.—*William C. MacCarty, Jr., M.D.*

McClure, Richard F., and Wahby, Elmer F. Developmental abnormalities of the duodenum producing obstruction. *Radiology*, Oct., 1953, *61*, 516–522.

Congenital obstructing lesions of the duodenum may be classified as follows:

I. Intrinsic
   A. Atresia
   B. Stenosis
II. Extrinsic
   A. Persistent cholecystoduodenocolic membrane
   B. Abnormal fixation of the duodenum permitting volvulus
   C. Annular pancreas or aberrant pancreatic tissue
   D. Vascular anomalies
   E. Prenatal development of mesenteric cysts
   F. Cysts of the liver or pancreas.

The embryology of the duodenum is described. Congenital anomalies of the duodenum do not develop as such; they exist because, at one stage or another, the normal development is arrested.

Congenital obstructing lesions of the duodenum producing atresia and stenosis have been frequently reported. The clinical picture is one of intestinal obstruction wherein bile-stained vomitus points to a site below the ampulla of Vater, bile-free vomitus indicates obstruction above the ampulla, and bile-

free vomitus plus bile-free stools suggests complete duodenal atresia. A case report and roentgenographic reproductions of an infant demonstrating atresia proximal to the ampulla of Vater are presented.

The most common extrinsic cause of obstruction is the cholecystoduodenocolic membrane often referred to as a "duodenal band." This may cause obstruction in infants and adults. The roentgen deformity consists of (a) constriction of the anterosuperior surface of the duodenal bulb; (b) a feathery irregularity of one surface of the bulb with opposing surface appearing smooth; (c) irregularity of the pyloric antrum and sphincter; (d) high fixation of the duodenal bulb associated with a dilated ptotic stomach. Four such cases are reported with reproductions of descriptive roentgenograms. Although present at birth, the duodenal band may produce only vague symptoms until adulthood, at which time obstruction may occur. Such a band may resemble a duodenal ulcer deformity.—*Everett E. Seedorf, M.D.*

NIXON, H. H. Meconium ileus; a report of a successfully treated case and a study of the surgical aspects of a series of 14 cases. *Brit. J. Surg.*, Sept., 1953, *41*, 184–188.

The author reports an infant girl with meconium ileus who was treated successfully by surgery. The patient began vomiting at twelve hours of age and developed progressive distention of the abdomen with visible small bowel peristalsis.

Roentgenograms of the abdomen revealed dilated small intestinal loops with fluid levels and mottled densities throughout the lower abdomen suggesting meconium ileus as the probable cause.

Surgical exploration revealed dilated loops of small intestine which tapered to an unexpanded terminal ileum which joined a completely unexpanded and normally fixed colon. Decompression was achieved by means of a small Paul's tube tied into the apex of the loop, after the insertion of pancreatin granules.

After operation 15 per cent pancreatin solution was instilled into the enterostomy twice daily to dissolve the meconium plug. The patient began to pass meconium. An extraperitoneal closure was attempted fourteen days after the initial enterostomy which broke down. Slight leakage persisted to the tenth week, when it ceased, leaving a sound scar.

At the age of six months the pancreatin was stopped for two days and the child produced the typical offensive stools of fibrocystic disease of the pancreas. A specimen of duodenal juice showed no tryptic activity at a dilution of 1 in 6 and a stool diluted 1 in 12 also failed to digest gelatin.

The patient weighed 35 pounds at three years of age.

The author discusses the diagnosis, treatment and prognosis of meconium ileus in the light of a series of 14 cases.—*James F. Martin, M.D.*

GAY, BRIT B., JR., LEIGH, TED F., and ROGERS JAMES V., JR. Abdominal aneurysm as an uncommon cause of duodenal loop widening. *Radiology*, Oct., 1953, *61*, 630–632.

Causes for compression and widening of the duodenal arc have been tabulated as follows:

1. Carcinoma of the head of the pancreas
2. Enlargement of lymph nodes in the region of the pancreatic head, due to:
   (a) Lymphoma
   (b) Metastases
   (c) Inflammatory disease (tuberculosis, infectious mononucleosis)
3. Edema of the pancreas in biliary diseases
4. Chronic pancreatitis
5. Other retroperitoneal tumors, as sarcomas
6. Cysts of the head of the pancreas
7. Aneurysms of the anterior wall of the abdominal aorta
8. Amyloidosis of pancreas
9. Upward traction on the duodenum as in hiatus herniation of the stomach.

The authors report 3 cases and include descriptive roentgenographic reproductions in which abdominal aneurysm was the cause of widening of the duodenal loop.

Roentgen examination in most cases will permit differentiation of vascular and nonvascular lesions in this region. Routine abdominal roentgenograms will show the presence of a soft tissue mass with curvilinear peripheral calcifications and occasional vertebral erosion allowing a diagnosis of aneurysm in most cases. Vascular lesions can be definitely excluded by aortography.—*Everett E. Seedorf, M.D.*

MANDL, F. Zur präoperativen Cholangiographie. (Preoperative cholangiography.) *Wien. klin. Wchnschr.*, Oct. 16, 1953, *65*, 876–877.

The author reports on 10 patients, in 4 of whom his method was not applicable. In the 6 patients examined the cholangiographic diagnosis was confirmed by the results of surgical exploration.

Under anesthesia and after paralyzing the diaphragmatic motion by means of a curare preparation, the author inserts a lumbar puncture needle into the liver at the external margin of the rectus muscle 3 fingers below the costal arch, aspirating all the while until bile appears in the syringe. He then injects 20 cc. of a 35 per cent iodide opaque medium ("ioduron"). After the injection the needle is withdrawn and a roentgenogram is made.

On the basis of these 6 cases the author concludes that "the diagnostic premises have been fulfilled."—*Albert Oppenheimer, M.D.*

Frommhold, W. Ein neuartiges Kontrastmittel für die intravenöse Cholezystographie. (A new contrast medium for intravenous cholecystography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Sept., 1953, *79*, 283–291.

"Biligrafin" is a sodium salt of triiodophenylcarbonic acid and contains 64.32 per cent iodine compared to 52 per cent in biliselectan. The higher iodine content leads to denser contrast shadows. The drug produces no or little gastrointestinal irritation. The finer branches of the biliary tract (intrahepatic) are frequently demonstrated to good advantage, especially if the normal dose of 20 cc. of a 20 per cent solution is doubled. As in other intravenous procedures, the gastrointestinal tract may be simultaneously examined in the routine manner.—*J. Zausner, M.D.*

Hornykiewytsch, Th., and Stender, H. St. Intravenöse Cholangiographie. (Intravenous cholangiography.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Sept., 1953, *79*, 292–309.

Biligrafin was injected in 274 patients whose biliary tracts were being investigated. Prior to the injection, each patient is prepared by a water enema (patient is in right lateral recumbent position); and a test for iodine sensitivity is made. The injection is made rather slowly, 20 cc. in 3 minutes, or 30–40 cc. in 5–6 minutes. Excretion studies show that 90 per cent of the opaque medium is eliminated by the liver and 10 per cent by the kidneys unless liver damage is present. The average examination includes 4 roentgenograms: 20–25 minutes after start of injection; 1 hour after injection; 2–2½ hours after injection; and one after a motor meal or magnesium sulfate. If the gallbladder itself is of primary interest, the last two roentgenograms will suffice but the authors strongly recommend the entire series. The examination is of doubtful value in the presence of profound jaundice. The opaque medium is fairly well tolerated: 6 per cent of the cases had mild symptoms, 1 per cent had moderately severe reactions despite negative sensitivity tests.

In normal patients, during the initial phase the intra- and extrahepatic biliary tree is shown in the first roentgenogram. As the ducts become barely visible, the gallbladder shadow becomes more prominent, and after 2 hours the concentration of the opaque medium is at its maximum. After 12–24 hours, all the contrast material is in the large intestine.

The presence of gallstones decreases the intensity of the gallbladder shadow, so that adequate visualization may not be reached for 2 hours. The hepatic and common bile ducts are well filled if the sphincter of Oddi is spastic but poorly visualized if the sphincter is insufficient. Dilatation of the large ducts is found in cases of cholelithiasis with cholangitis, or in the latter condition alone. The ducts are especially well demonstrated when a large stone obstructs the infundibulum of the gallbladder. In cases with a long-standing icterus, there may be no visualization of the biliary tract.

In patients with cholecystitis and cholangitis, the following three possibilities arise: (1) The gallbladder and biliary ducts appear normal. (2) The gallbladder is slowly and poorly visualized; the ducts are well demonstrated for a prolonged period or poorly seen for a short while. (3) The gallbladder is not filled; the filling of the ducts depends on the status of the sphincter of Oddi. In the last case, the gallbladder or the cystic duct is the site of inflammatory edematous, or scarred changes. If the sphincter tone is high, the ducts will be well filled; if low, the contrast medium passes rapidly into the intestines. Occasionally, despite inflammatory changes in the cystic duct, the gallbladder will fill fairly satisfactorily after 1–2 hours.

The cholecystectomized cases are divided into four groups: (1) normal, undilated ducts and normally functioning sphincter of Oddi—asymptomatic; (2) spastic changes in the distal portion of the common bile duct—occasional colicky pains due to recurring spasms in the antrum or distal portion of the common bile duct; (3) appreciable dilatation of the common bile duct and a spastic sphincter—symptoms disappear after sphincterotomy. Adhesions or diverticula are other causes for dilatation; (4) insufficiency of the sphincter due to inflammation or operative interference of the sphincter.

The intravenous method offers a better understanding of the functional as well as morphological and pathological characteristics of the biliary system. —*J. Zausner, M.D.*

Grugan, Robert A. An oral cholecystographic method using telepaque with demonstration of the common and cystic ducts. *Radiology*, Oct., 1953, *61*, 633–636.

The author reports visualization of the cystic and common bile ducts in 91 per cent of a series of 132 patients given 3 grams of telepaque. The important factor in technique is that the duct-filling roentgenograms must be made 15 to 20 minutes after administration of a fat meal. Within 45 minutes the opaque medium may already be expressed from the biliary ducts.

Calculi have been demonstrated within the cystic and common duct and the size and anatomic relationships of the ducts can be evaluated.—*Everett E. Seedorf, M.D.*

Birsner, J. W., Wallner, A., and Leask, William H. Roentgen diagnosis of rupture of the spleen by pneumoperitoneum. *J. Internat. Coll. Surgeons*, Sept., 1953, *20*, 338–341.

The authors advocate the use of four roentgenograms of the abdomen (in the supine, erect, and right and left lateral decubitus) after injection of 350–400 cc. of air. Air is used to permit serial roentgenograms at intervals of about twelve hours, if necessary, and to avoid more rapid absorption which might occur with use of oxygen or carbon dioxide.

Three patients are reported with correlation of irregularity of the splenic shadow and splenic injury. Two of these who required operation showed splenic injury.

This technique may reveal irregularity suggestive of subcapsular hematoma or abnormal soft tissue between the spleen and lateral abdominal wall. Free fluid, such as blood in the peritoneal cavity, may show as a fluid level.

Similar use of this technique is advocated for evaluation of possible traumatic laceration of the liver.—*John W. Turner, M.D.*

Genitourinary System

Moore, Thomas D., and Sanders, Nelson. Reaction to urographic agents with and without antihistamines. *J. Urol.*, Sept., 1953, *70*, 538–544.

This article is an investigation covering 510 patients given one of five intravenous preparations for roentgen diagnosis of the urinary tract. These preparations were diodrast, methyl glucamine salt, diodrast with benadryl, diodrast with thenfadil and the sodium salt of (1–3,5-diiodo-4-pyridone)-propanoate.

The authors have reached the conclusion that the methyl glucamine salt appeared to be somewhat better tolerated than the diethanolamine salt. The latter is the commercial diodrast. The use of a potent antihistamine with diodrast appears to offer some advantages from the standpoint of reduction of side effects. No severe reactions were encountered, excepting with the sodium salt of (1–3, 5-diiodo-4-pyridone)-propanoate.—*George W. Chamberlin, M.D.*

Hansen, Poul Bjerre. Sympathicoblastoma of the adrenal medulla with osseous metastases; a report of three cases including one surviving eleven years after roentgen therapy. *Acta radiol.*, Nov., 1953, *40*, 500–510.

Three cases of sympathicoblastoma with osseous metastases are reported. One child survived for eleven years after roentgen therapy to extensive osseous metastases. There is a detailed discussion on therapy and prognosis.—*C. Peter Truog, M.D.*

Skeletal System

Richards, H. J. Parathyroid osteodystrophy; report of a case. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 593–597.

The patient reported in this paper is a woman, aged sixty-nine, who was admitted to the hospital for a fracture of the neck of the left femur sustained while she was mounting the stairs in her home. During routine manipulation to reduce the fracture of the femoral neck, a spiral fracture of the shaft of the femur was produced. At the subsequent nailing operation it was noted that the bone was abnormally soft. A biopsy was taken but the pathological examination showed no conclusive findings.

The blood calcium was 11.3 mg. per cent, phosphorus 2.9 mg. per cent, alkaline phosphatase 25 units. Blood picture was normal except for diminished hemoglobin value (70 per cent). Blood urea was 30 mg. per cent and plasma proteins 6.5 per cent. Two sternal punctures gave findings suggestive of multiple myelomatosis.

Three months later the blood calcium had risen to 13.6 mg. per cent and complete roentgenographic examination showed generalized osteoporosis with cystic changes in several bones consistent with osteitis fibrosa cystica. The neck was explored at operation and a large tumor of the right superior parathyroid gland was removed. Macroscopically the specimen showed general hyperplasia of the gland without evidence of a localized adenoma. Microscopically, the cells were all of a pale, oxyphil type. There were a few cells with exceptionally large hyperchromatic nuclei.

When the patient was reviewed two years and three months after operation she had made good progress: the fractures of the femur had united and the cystic lesions of the bones had filled in, but considerable osteoporosis was still present. She was in good health and walked with the aid of a cane.

Although the diagnosis of parathyroid osteodystrophy was suspected at the time of the nailing operation, the serum calcium was at that time within normal limits and there were a number of unusual features that threw doubt on the validity of that diagnosis. It seems possible that the history extended back forty-nine years to the time when the patient first developed symptoms of aches and pain in her bones, anemia, and signs of peptic ulceration at the age of twenty. Norris, quoted by the author, concluded that the duration of parathyroid osteodystrophy was much longer than was generally realized and he reported one case of thirty-nine years' duration. Anemia is common in all conditions associated with hypercalcemia. Gastric and duodenal ulcers in association with hyperparathyroidism have also been reported. Snapper has reported the presence of Bence-Jones bodies in the urine such as were found in the case reported in this paper.—*Ralph S. Bromer, M.D.*

Aigner, Rolf. Ueber Osteopoikilie verbunden mit Keratoma hereditarium dissipatum palmare et plantare (Brauer). (On osteopoikilosis associated with hereditary disseminated

palmar and plantar keratoma [Brauer].) *Wien. klin. Wchnschr.*, Oct. 9, 1953, *65*, 860–862.

This is a case report of a girl, aged fourteen years, in whom osteopoikilosis ("spotted bones") coexisted with skin changes that were consistent with disseminated palmar and plantar keratoma. The same abnormalities were found in one of the patient's sisters, while the other members of the family did not present the same combination of findings.

The author concludes that the two morbid conditions are related genetically and morphologically.—*Albert Oppenheimer, M.D.*

James, J. I. P. Tuberculosis transmitted by banked bone. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 578.

The use of banked bone is becoming general but there are few reports of complications. At many hospitals an adequate supply of bone has been difficult to obtain and the use of ribs removed for thoracoplasty in pulmonary tuberculosis has become common.

The author reports 4 cases of tuberculous abscesses which were discovered after the use of ribs from thoracoplasties performed in cases of pulmonary tuberculosis. Such ribs had been used for various orthopedic procedures. The ribs were frozen at −15° C. to −20° C. in a solution containing penicillin and streptomycin. After removal of the infected bone chips in the 4 cases and curettage, the wounds healed without further incident. It is, however, possible that further manifestations may appear.

The author believes that these unfortunate sequelae make it obvious that such material is not suitable for bone graft.—*Ralph S. Bromer, M.D.*

Fairbank, H. A. Thomas. A parosteal lipoma. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 589.

This paper is a short case report of a lipoma causing a lesion of the posterior interosseous nerve, without, however, interference with its function. There was an obvious swelling on the outer side of the forearm in the upper third. The roentgenogram showed a bilobed radiolucent tumor adjacent to the upper third of the radius.

Fairbank quotes D'Arcy Power who used the term "parosteal" when he reported a case of lipoma growing beside a femur. Bland-Sutton cited 14 cases, including 1 of his own of "parosteal lipomata" which he regarded as arising from the periosteum. In only 1 case was there involvement of the bone. Fairbank thinks "parosteal" seems to be preferable to "periosteal" as applied to these lipomas and both terms seem to be more accurate than "subperiosteal."—*Ralph S. Bromer, M.D.*

Drey, L. Failure in modeling of bone. *Radiology*, Oct., 1953, *61*, 645–648.

The process of bone growth is influenced by two main and complementary factors: (1) the regulation of longitudinal growth by the metaphyseal cartilage and (2) the shaping of bone by the periosteum. These two factors are synchronized in their action. When this normal process of modeling is disturbed, the bone continues its growth in a straight line and is broadened in a club-like form at the metaphysis, losing the tubular shape of normal bone.

This failure in modeling is present in several diseases of bone in which normal coordination of cartilaginous growth and periosteal bone shaping is interrupted. The club-like metaphyseal swellings of Gaucher's disease and Cooley's anemia are examples of abnormal modeling of bone due to failure in the normal function of the periosteum. Disturbance of the normal calcification of the metaphyseal cartilage in rickets also causes a metaphyseal broadening which may be due to "undertabulation" or to "underconstriction." A similar deformity occurs in osteomyelitis.

The pathological broadening of bone at the metaphysis is not pathognomonic of any one disease. The same deformities of bone are observed in such different pathological entities as Gaucher's disease, Cooley's anemia, osteomyelitis and rickets.—*Arno W. Sommer, M.D.*

Costa, Asdrubal, and Da Gama, Jayme. Contribuição ao estudo das alterações ósseas da carência vitamínica A na infância. (Contribution to the study of bone changes in vitamin A deficiency in infancy.) *O Hospital*, Nov., 1953, *44*, 633–660.

After presenting an extensive historical survey of vitamin A deficiency the symptoms of which have been described in the medical and religious literature of the world for almost 2,000 years, the authors describe 26 cases of their own.

All of these cases showed, in varying degrees, the four principal roentgen signs of vitamin A deficiency in long bones: (1) generalized osteoporosis, (2) condensation of the zone of preliminary calcification or epiphyseal plaque, (3) transverse lines of increased density in the diaphyses of long bones, and (4) retardation of the centers of ossification combined with deficiency in the longitudinal growth of the shaft of the long bones. It must be stated, however, that none of these roentgen signs can be regarded as absolutely pathognomomic for vitamin A deficiency since occasionally they may be found in other pathologic conditions.

The differential diagnosis involves particularly infantile scurvy, rickets and congenital lues. Osteochondritis, osteomyelitis, and other infections, erythroblastosis and other blood dyscrasias must also be considered.—*Ernst A. Schmidt, M.D.*

BINGOLD, A. C. Congenital kyphosis. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 579–583.

The author's purpose is to give an account of congenital kyphosis based on a study of 3 cases and a survey of the literature. Congenital kyphosis is of two types: the first is associated with widespread disturbance of ossification, and is seen in chondro-osteo-dystrophy, gargoylism, cretinism and achondroplasia; in the second, the kyphosis is due to localized malformation of the spine and the rest of the skeleton is normal. The second type alone is discussed in this paper.

The cause of the condition is unknown. Except for two brothers with lumbodorsal kyphosis no familial examples are known. The roentgenographic features show that there may be up to five abnormal vertebrae. The kyphosis has been observed between the fourth thoracic and the fourth lumbar vertebrae. The defect may consist in: (1) absence of the body of the vertebra; (2) absence of the body of the vertebra associated with microspondyly of a neighboring vertebra; (3) microspondyly of one vertebra; (4) microspondyly of two neighboring vertebrae; (5) incomplete segmentation of neighboring vertebrae; (6) absence of a corner of a vertebra; and (7) wedging of a vertebra in the lateral view which is associated with a butterfly appearance in the anteroposterior view.

Two complications may arise. Osteoarthritis may develop and cause pain. The second complication is damage to the nervous system such as flaccid paralysis of the legs, paralysis of the interossei of the feet and bladder insufficiency. The only difficulty in differential diagnosis arises if the condition occurs in a patient who has a history of tuberculosis in the family. If the patient has a consistently normal pulse and temperature and a normal blood picture, and if roentgenograms show one of the above abnormalities without osteoporosis, destruction of bone or a disc, or paravertebral abscess shadow, the diagnosis of congenital kyphosis is probably correct.—*Ralph S. Bromer, M.D.*

WILSON, J. N. Tuberculosis of the elbow; a study of thirty-one cases. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 551–560.

This paper is based on a study of 31 cases of tuberculosis of the elbow, 2 patients having had bilateral involvement. An attempt is made to classify the condition and to assess the results of treatment. The disease was commonest in the second and third decades of life.

Tuberculosis of the elbow is divided by the author into four main presenting types. Three of his cases could not be classified because the original roentgenograms had been lost. The four types of lesions in order of percentage of involvement are: the synovial, 9 per cent; the extra-articular, 18 per cent; the coronoid, 24 per cent; and the massive, 40 per cent. Nine per cent could not be classified.

A case of the synovial type is illustrated by roentgenograms which show, five years after onset and treatment, the joint space well preserved; clinicallly the patient had only terminal limitation of movement.

The extra-articular lesion occurred as the presenting lesion in 6 cases. The sites of the lesion in the 6 cases were: the medial epicondyle, the lateral epicondyle, the olecranon, olecranon and lateral epipcondyle, and the medial and lateral epicondyle. In the epicondylar lesions the prognosis was more favorable and in all the cases of this epicondylar type a considerable range of movement was restored.

The coronoid type is strictly an extra-articular lesion, but the author considers it under a separate heading since it differs from other extra-articular lesions in that the joint always becomes involved eventually. The focus usually lies just under the articular surface of the coronoid and extends slightly into the olecranon.

The massive lesion (involving all joint surfaces) was the most common type of the series. It is possible that in all these cases the earliest focus was of the coronoid type. It is not uncommonly associated with posterior displacement of the head of the radius. In 3 cases there was a complete dislocation. In both the coronoid and massive cases the prognosis for useful movement at the humero-ulnar joint was poor. The final results varied from complete bony ankylosis to a range of a few degrees of movement. However, a useful range of rotation was often obtained.

The complications of the series were: sinuses in 19 per cent, other tuberculous lesions in 40 per cent, and ulnar nerve paresis in 6 per cent (2 cases). Wilson thinks, however, that it is difficult to say whether ulnar nerve paresis is a true complication of the disease.

The operative treatment consisted of local excision of the lesion, excision of the joint, and arthrodesis. Predominantly conservative treatment, is preferred.

Of 20 patients observed for five years or more, 17 returned to work, 7 required permanent splintage and 5 had residual pain or sinuses. Fixation of the elbow at 30 degrees below the right angle is advised as the best position.—*Ralph S. Bromer, M.D.*

RUBINSTEIN, MICHAEL A., SMELIN, AMMIEL, and FREEDMAN, ALBERT L. Osteoblasts and osteoclasts in bone marrow aspiration; previously undescribed cell findings in Paget's disease (osteitis deformans). *A.M.A. Arch., Int. Med.*, Nov., 1953, *92*, 684–696.

The authors found two previously undescribed cells in bone marrow aspirates in 8 consecutive cases of Paget's disease. The involved illia were the sites used for aspiration. The most prevalent cell type is

the mononuclear one. These cells are large (25 to 50 μ in greatest diameter), ovoid in shape, and have hazy ill-defined cytoplasmic borders. The cytoplasm to nucleus ratio is about 3:1, which is greater than for most tumor cells. The nucleus is located eccentrically and often appears to be partly extruded from the cytoplasm. The nucleus stains purple and the cytoplasm gray-blue to deep blue with Wright's stain. There are several clear blue nucleoli. These cells may occur individually or in groups.

The other cell type is the syncytial one and these cells are multinuclear. The cells may reach over 200 μ in diameter and contain as many as 100 nuclei. The nuclei are irregularly distributed throughout the cytoplasm. There is much less cytoplasm than in the mononuclear type.

The above cells probably have not been reported in cases of Paget's disease before for the following reasons: The aspirations were not made where the disease was present, the unusual cells may have been regarded as plasma cells, and the aplastic marrow where these cells occur may have been discarded as unsatisfactory specimen. These cells are not pathognomonic of Paget's disease, as they have been found in other conditions, such as in a case of osteoblastic metastases secondary to breast carcinoma, in a case of anemia (probably Cooley's) in a child, in a case of osteosclerosis secondary to myelogenous leukemia and in a case of uremia, with secondary hyperparathyroidism.

Osteitis deformans is characterized by accelerated bone resorption and bone repair. The initial lesion is bone destruction produced by an unknown localized factor. In this phase numerous osteoclasts are seen. Due to secondary stresses and strains, osteoblastic activity is increased. The above process results in a "mosaic" structure. The histopathology of the involved bone includes a marked fibrosis, and the thickened and distorted bone trabeculae are lined with increased numbers of osteoblasts and osteoclasts.

The authors express the opinion that the mononuclear cells correspond to tissue cells described as osteoblasts by the histopathologists and the syncytial cells to osteoclasts. They conclude that finding these cells in bone marrow aspirates may help to confirm or suggest the presence of Paget's disease and certain other conditions. The two types of cells should not be confused with tumor cells.—*Charles W. Cooley, M.D.*

Otenasek, Frank J. The variety of spinal lesions simulating the disk syndrome. *South. M. J.*, Sept., 1953, *46*, 843–846.

The author presents 7 cases of neoplastic processes which closely simulated the clinical lumbar disc syndrome. In most instances the symptoms were typical of a herniated disc and in some there was roentgenological evidence of narrowing of the disc space. Myelography was not done before the original operation, and the finding of tumor was unexpected.

It is recommended that the following symptoms or findings in an otherwise typical disc case should call for more extensive studies including opaque myelography: night pain, persistence of pain without remission, root pain higher than L-5, alteration of the knee-jerk, bladder symptoms, and failure to obtain relief following the removal of a disc.

The article includes microphotographs of the various neoplastic processes which produced the atypical disc syndrome.—*C. L. Hinkel, M.D.*

Somerville, E. W. Development of congenital dislocation of the hip. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 568–577.

The views expressed in this paper are based on the findings at open operation in 35 congenital dislocations of the hip. In 3 hips (2 patients), the capsule was adherent to the femoral head which was pitted and irregular. The acetabulum was filled with dense fibro-fatty tissue which was adherent to the articular cartilage. It was difficult to reduce these dislocations. One of these patients had bilateral club feet and club hands but the other had no other congenital anomalies. These findings would fit the type of dislocation called "teratological." The appearance was quite different from that found in the remaining 32 hips which were classed as "typical dislocations." It is the latter type which is discussed in this paper.

The occurrence of dislocation of the hip is probably a gradual process spread over a considerable time, the stage of subluxation being passed through before dislocation is finally established. Whether it develops before or after birth is uncertain.

One sign in this series was a consistent finding. The limbus was found to be inverted into the joint in all the hips explored for complete dislocation, and was found not inverted in the one hip explored in which there was only a subluxation. That the limbus is inverted in dislocations can also be regularly demonstrated by arthrography. Whether large or small, it is always posterior, extending forward and involving the upper lip of the acetabulum to a variable extent. In some hips which are dislocated, Fairbank has shown that this posterior lip is large enough to have a facet on it and illustrated that it is within the joint capsule. Somerville suggests that the straight overhanging posterior lip, large enough to contain a facet and all intracapsular, is in fact the inverted limbus which has not—as is commonly supposed—atrophied, but has undergone ossification.

The limbus is a fibrocartilaginous rim attached to the margin of the acetabulum, which it deepens. In the congenitally dislocated hip, the limbus is found turned into the joint to a varying extent, forming a white, glistening crescent, like the meniscus in the knee. It lies in the posterosuperior position in the acetabulum and is sometimes only a thin outer rim.

Based on the tendency with which the limbus is

inverted into the joint in a typical congenital dislocation of the hip, Somerville advances the hypothesis which suggests that the sequence of events leading to established dislocation is: (1) lateral position aided and abetted by anteversion; (2) extension of the hips causing subluxation; (3) dislocation and inversion of the limbus; (4) secondary changes in the upper end of the femur, pelvis and acetabulum which will also develop if the deformity does not progress beyond a subluxation. He also describes how anteversion of the neck is either moulded away during growth to produce a normal hip, or persists with or without dislocation. If this sequence of events is correct, it should be possible, up to the time when secondary changes are irreversible, to obtain a good result in just so long as is required to turn the limbus out of the joint and permanently to prevent the laterally rotated position at the hip. While early removal of the inverted limbus has the advantage of producing a relatively normal acetabulum as quickly as possible, it has the disadvantage of not allowing sufficient time to elapse for the anteversion to correct itself naturally if it is going to, and a rotation osteotomy must be done to reduce the time of immobilization to the minimum.—*Ralph S. Bromer, M.D.*

LANDELLS, J. W. The bone cysts of osteoarthritis. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 643–649.

Landells states that rounded areas of translucency in the bones forming an osteoarthritic joint are well known to radiologists and to orthopedic surgeons. These areas are found in relation to defects in the water-tight layer between the joint space and the cancellous bone. They are sometimes obvious openings, but are more often openings closed by fibrous tissue, fibrocartilage or new bone. The small cystic areas lie close to the surface. Their rounded outlines suggest fluid pressure as a factor in their formation. The fluid and cells found in the cysts are compatible with an origin in the joint space and articular cartilage.

Landells advances the hypothesis that the cysts are formed by the intrusion of synovial fluid under pressure into the substance of the bone, and that the sclerosis around them is the result of displacement of the trabeculae and their reinforcement by new bone. Such sclerosis around the cysts is one of their most conspicuous features and is difficult to explain on a hypothesis of degeneration as a cause. The view that the fibrous and myxomatous changes are primary, leading to accumulation of fluid and thus to cyst formation involves several difficulties. Concentric zones of fibromyxomatous changes in the marrow and bone-forming reaction would seem to be improbable. The presence of living cartilage derived from the articular surface in open fluid-filled cysts, and of dead cartilage in the fibrous tissue constitutes further argument against this last-mentioned hypothesis.—*Ralph S. Bromer, M.D.*

LLOYD-ROBERTS, G. C. The role of capsular changes in osteoarthritis of the hip joint. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 627–642.

This study is based upon an operative and histologic study of 25 osteoarthritic hips subjected to arthroplasty or arthrodesis. In no case did infective, rheumatoid or ischemic factors determine the onset or complicate the condition. The youngest patient was forty-nine years of age, the oldest seventy-three. In particular, the synovial membrane and capsule were studied.

Fragments of bone and cartilage were found beneath the synovial surface in 23 of the 25 cases of osteoarthritis. The source of these fragments was the degenerate articular surface. Fibrosis of the synovial membrane and capsule followed the synovial hyperplasia which accompanied the phagocytosis of these fragments. The greatest amount of the joint debris was found in the lowest part of the joint cavity. It seemed that the joint capsule was particularly sensitive to traction. All parts of the capsule were tight in extension which is the weight-bearing position. Fibrotic shortening of the capsule can explain, according to Lloyd-Roberts, many of the symptoms and signs of the disease. Pain is caused by an attempt to stretch the capsule. Spasm occurs in the muscles supplied by the sensory nerves of the joint capsule in the lowest part of the joint cavity. Subperiosteal new bone is formed on the undersurface of the neck of the femur.

Evidence of capsular shortening is provided by a roentgen sign. This is new bone formation visible below the femoral neck which was seen in 33 out of 73 consecutive patients with osteoarthritis of unknown origin subjected to operation. The new bone formation is regarded as a buttress formed in response to abnormal stress. Lloyd-Roberts believes that this bone is subperiosteal and is caused by elevation of the periosteum away from the neck of the femur by a traction force transmitted through the posteroinferior capsular reflection.—*Ralph S. Bromer, M.D.*

HARRISON, M. H. M., SCHAJOWICZ, F., and TRUETA, J. Osteoarthritis of the hip: a study of the nature and evolution of the disease. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 598–626.

The hip joint was selected by the authors for this investigation of osteoarthritis because it is the commonest clinical site of severe osteoarthritis. The investigation embraced not only the disorganized joint of the final phase of the disease but also the various stages of its evolution from the normal. The authors' description is limited, largely by considerations of length, to the femoral head. They found that the changes in the acetabulum are similar and like mirror

images of those occurring in the head of the femur, the other member of the articulation.

The material of the investigation consisted of 91 postmortem examinations of the hip, 45 femoral heads removed at operation from osteoarthritic hips, and roentgenograms from 80 selected patients suffering from osteoarthritis of the hip in whom it was possible to follow the progress of the disease over several years.

The first section of the paper is concerned with considerations of the anatomy of the hip joint. The distribution of pressure and nonpressure areas commonly present in the normal adult femoral head is described. It seems probable to the authors that the duration of weight bearing, habits of stance, and the relatively restricted joint usage of adult life, as opposed to those of youth and adolescence, may explain the tendency to increasing definition of the pressure system in the human. This concentration of the load explains the thinning of the trabeculae in the lightly stressed segment of the head, particularly that part which is opposed to the acetabular fossa.

In considering the results of their study, the authors first discuss the nature, frequency and distribution of the cartilage lesion. Osteoarthritis, as seen in the hip, is a disease which eventually embraces all the tissues of the joint but which begins as a reaction of the juxtachondral blood vessels to a degeneration of the articular cartilage. This reaction results in a hyperemia of the bone. The degree of cartilage degeneration was not uniform within the imprint of the acetabular fossa in any one femoral head. It was usual to find the cartilage of the pressure area in an excellent state of preservation. The authors noted, to their surprise, that daily use preserves rather than "wears out" articular cartilage. Inadequate use is the commonest cause of articular degeneration and ensuing vascular invasion. To this factor are added the effects of excessive pressure in the many patients who require surgical treatment for advanced osteoarthritis of a hip, the seat of some anatomical incongruity. This etiology based on cartilage involvement, explains, too, the osteoarthritis implanted on joints of a normal shape which have been previously affected by acute or chronic inflammation or by hormonal dysfunction, such as acromegalic osteoarthritis. The stimulus to vessel growth and invasion is the same in all these cases, namely, cartilage damage.

A section is devoted to the topography and vascular anatomy of the osteophyte. The earliest osteophytes visible are those found at the junction of articular cartilage and synovial membrane. On the femoral head such junction occurs at the margin of the fovea capitis medially and at the periphery of the articular cartilage laterally. The origin and growth of an osteophyte depends upon the proliferation of blood vessels into the degenerate articular cartilage and intracapsular vascularization. As an osteophyte increases in size, its growth is preceded by the intracartilaginous spread of the original penetration and by the appearance of new vessels from whichever source did not contribute initially. These groups of vessels and the bone they form gradually tend to coalesce. What is so damaging in osteoarthritis seems to be not the degeneration of the cartilage but the vigorous and persistent attempt at repair, an attempt which aggravates the already disordered function of the joint not only by osteophyte formation but by the hypervascularity which weakens the structure of the bone beyond the point where it can carry its increased load. The collapse which follows provokes further reparative efforts with the same ill results.

In the discussion of the destructive phase of the disease, flattening of the femoral head is described. As osteoarthritis develops in the hip, there is a progressive increase in the load that a part of the joint is called upon to bear. The bony architecture of the head, rarefied and weakened by the hyperemia, receives this increased load the crushing effect of which is heightened by the progressive loss of resilient articular cartilage from the pressure area. The head starts to decrease in height from successive trabecular fractures, and the top of the femoral head becomes flattened.

The authors apply the term cysts to those translucent areas which may be seen in clinical roentgenograms. Every osteoarthritic head removed at operation in the authors' series contained cysts. The cysts are frequently cup-shaped or pyriform but sometimes they may be seen as discrete spherical lesions within the bone, separate from the joint cavity. The bony wall of a cyst is formed by thickened trabeculae.

Necrotic bone is found on the surface of the pressure area. The necrotic bone and marrow may remain but little changed, or they may be ground into bone "sand" or they may be the site of osteoclastic removal and osteoblastic replacement. The commonest situation for necrotic bone is within and between the cysts. The presence of calcified cartilage upon the surface shows that the flattening of the head is not due to a wearing away but is really an impression.—*Ralph S. Bromer, M.D.*

Tupman, G. S. A case of tuberculosis of the ischium. *J. Bone & Joint Surg.*, Nov., 1953, *35-B*, 590–592.

Tuberculosis of the ischium is rare. A case is reported of a girl, aged twenty years, who complained of aching pain in the groin. Roentgen examination revealed a suspicious area of rarefaction in the right ischial tuberosity with evidence of sequestration. The roentgenogram of the lungs showed a healed tuberculous lesion in the right apex. The diagnosis of tuberculous abscess was confirmed by the aspiration of 350 cc. of thin yellow pus containing acid-fast bacilli. A later roentgenogram of the right ischium showed a large cavity containing sequestra. The sequestra were removed at operation and local strep-

tomycin was instilled in the drainage tube. The wound healed by first intention and the patient had remained well, one year after the operation.—*Ralph S. Bromer, M.D.*

BLOOD AND LYMPH SYSTEM

DE WINTER, JAN G. Alcohol-induced pain in Hodgkin's disease. *Brit. M. J.*, Sept. 12, 1953, *2*, 604–605.

The author, reporting from the Royal Sussex County Hospital in Brighton, describes a seldom observed phenomenon, only twice previously recorded.

The phenomenon consists of acute pain following the ingestion of alcohol- containing beverages in certain cases of Hodgkin's disease. The pain, when it is encountered, is localized to the particular part of the body involved by the disease and in this way it appears to have a certain degree of usefulness in "pinpointing" lesions which might otherwise remain unrecognized.

The author recommends the institution of a "diagnostic drink" in the evaluation of new cases of Hodgkin's disease and at follow-up visits.

It is interesting to note that the pain has been found to disappear following successful irradiation.—*C. L. Hinkel, M.D.*

WYLIE, EDWIN J., and MCGUINNESS, JOSEPH S. The recognition and treatment of arteriosclerotic stenosis of major arteries. *Surg., Gynec. & Obst.*, Oct., 1953, *97*, 425–433.

This report is based on the clinical and pathologic characteristics of stenosis of major arteries due to arteriosclerosis in a study of 27 patients. All were males except two. The age distribution was as follows: 30 to 40 years, 5; 40 to 50 years, 12; 50 to 60 years, 8; and 60 to 70 years, 2.

In all patients, the pathologic changes involved a portion of the major arterial tree between the upper abdominal aorta and the level of bifurcation of the popliteal arteries.

Four categories of patients are included in this study: (a) 12 patients in whom a segmented zone of arteriosclerotic narrowing was the sole demonstrable cause for the presenting complaints of arterial insufficiency; (b) 6 patients in whom asymptomatic arterial stenosis was an incidental arteriographic finding; (c) 6 patients whose original stenotic lesion progressed to complete thrombosis; (d) 3 patients who were found to have a significant stenotic lesion apart from a separate zone of arterial thrombosis.

Vascular studies consisted of oscillometric recordings of the peripheral pulses at rest and after exercise, sound tracings of peripheral arterial murmurs, and arteriograms of the arterial tree from the upper abdominal aorta to the popliteal arteries.

Aortography Technique. The patient is placed prone over a cassette tunnel in which slots are provided for two 14 by 17 inch Lysholm wafer grids, and a 14 by 36 inch cassette. The roentgen tube is fitted with a rectangular cone and an aluminum filter tapered to permit equal penetration of the abdomen and the less dense extremities. Under general anesthesia, two 17 gauge, 7 inch needles are inserted, 1 inch apart, into the abdominal aorta proximal to the celiac axis. Fifty cubic centimeters of 70 per cent diodrast, or 70 per cent urokon, divided between 2 syringes, is injected manually over a 4 second interval through the two needles. Four 36 inch films are exposed serially over an 8 second interval. The factors for the average patient are 81 kv. (peak), 400 ma., and ½ second, at a distance of 6 feet.

A large volume of contrast solution (50 cc.), injected rapidly, has been found necessary to give adequate visualization. This is of particular importance if there are multiple levels of occlusive lesions. It is recognized also that accurate evaluation of the prognosis and operability requires a demonstration of the full length of the arterial tree from the level of the diaphragm to the lower legs.

The pathologic and arteriographic characteristics of the lesions encountered were found to be closely related. Significant changes in the lumen or the wall of the aorta were never observed proximal to the level of the superior mesenteric artery and in most cases only distal to the renal arteries. In those cases in which marked stenosis was found at a level between the renal arteries and the bifurcation of the common iliac arteries, the intima over this entire area was usually involved to a variable degree by arteriosclerotic thickening and plaque formation. It was unusual to find appreciable changes in the external iliac arteries, but when changes did occur there was usually diffuse involvement of the major arteries in the legs as well. The most marked degree of stenosis was usually observed near the orifice of a major arterial branch, *i.e.*, at the level of the inferior mesenteric artery or at the bifurcation of the aorta, common iliac, and common femoral arteries. In some, an annular "napkin ring" lesion was present. In others, an eccentric cylindrical thickening of one wall of the artery projected sufficiently into the lumen to create a crescent-shaped lumen when examined in cross-section. When the posterior wall of the artery was involved by eccentric thickening, the arteriographic picture showed decreased opacity rather than luminal narrowing.

Further pathologic observations and certain clinical and operative experiences have suggested that arterial stenosis of sufficient degree to cause symptoms is a predisposing lesion to the development of arterial thrombosis. Partially organized, clotted blood was frequently found adherent to the luminal surface of the intima at the level of stenosis. There were 6 patients in whom the original stenotic lesion progressed to complete occlusion. In 3 other patients, complete occlusion developed during an observation period following the arteriographic diagnosis of marked common iliac stenosis.

Other observations have suggested (1) that stenosis due to extraluminal thickening of the arterial wall represents an intermediary stage in the development of arteriosclerotic arterial thrombosis, (2) that the local intraluminal accumulation of clotted blood at the site of such a stenosis probably is a precipitating event in the development of complete occlusion, and (3) that the collateral flow of blood tends to limit the levels of proximal and distal extension of the subsequent intraluminal thrombus to the levels of major arterial branches.

The specimen obtained from the surgical resection of the thickened intima of an arteriosclerotic, stenotic artery is a hollow, inelastic cylinder. Measurements in cross-section at the point of greatest narrowing suggest that there is a critical degree of narrowing necessary to produce symptoms of ischemia. The normal cross-section area of the common iliac artery has been found to be 80 sq. mm. In the stenosed common iliac specimens, the average was 6 sq. mm. and was never more than 7 sq. mm.

The clinical findings in the patients of this series varied with the degree of stenosis, the length of stenotic segment, the level of the lesion in the arterial tree, and the presence or absence of occluding disease at the levels of the vascular tree distal to the stenotic zone. The patient with stenosis of the superficial femoral artery complained of calf claudication and chronic coldness of the foot. The patient with common femoral stenosis who later developed complete femoral occlusion, complained of severe fatigue of the posterior thigh muscles in walking, which limited his capacity to one-half block. The patients with unilateral common iliac stenosis described fatigue of the gluteal, as well as the thigh muscles, and frequently developed pain in the hip, produced by walking and relieved by rest. Bilateral common iliac stenosis produced the symptoms in both extremities and, in addition, was frequently associated with sexual impotence.

Summary. Arterial disease of sufficient degree to produce ischemic symptoms represents an almost complete arterial occlusion and is a frequent intermediary stage in the development of arterial occlusion. In 12 patients the stenotic lesion was localized to a short segment and amenable to direct surgery with restoration of a normal arterial lumen and relief of symptoms of ischemia in 10 patients. Prolonged expectant treatment may decrease the possibility for successful restoration of the arterial lumen.—*Robert K. Arbuckle, M.D.*

Walter, Robert C., and Goodwin, Willard E. Aortography and retroperitoneal oxygen in urologic diagnosis: a comparison of translumbar and percutaneous femoral methods of aortography. *J. Urol.*, Sept., 1953, *70*, 526–537.

The details of the technique of translumbar aortic puncture and of percutaneous femoral artery catheterization are included in this excellent article. Attention is called to the diagnostic value of the procedures as well as some pitfalls in interpretation. The advantages of the combined procedure of retroperitoneal oxygen plus aortography are demonstrated. In patients with lumbar aortic aneurysms or in some cases of severe scoliosis the translumbar method is contraindicated. In most other cases, however, it is the procedure of choice. The percutaneous femoral method may be contraindicated by peripheral vascular disease or in those patients with local lesions of the inguinal or femoral region.

The importance of a test injection of contrast medium with a scout roentgenogram as a preliminary step is emphasized. The advantages of serial roentgenograms are enumerated.—*George W. Chamberlin, M.D.*

Peisojovich, A., Nusimovich, B., and Vargas, Heredia. Granuloma paracoccidioídico Brasiliensis. (*Paracoccidioides brasiliensis* granuloma.) *Semana méd.*, Sept. 17, 1953, *103*, 424–426; and 438.

Two forms of this parasitic disease, very frequent in Brazil, are recognized. The tegumentary lymphatic form usually begins in the buccal, labial, nasal mucosa, infiltrates slowly, later ulcerating, and usually runs a chronic course. The visceral lymphatic form starts with an attenuated buccal lesion, rapidly followed by involvement of the cervical and supraclavicular lymph nodes, and from there it spreads to various internal organs. In Brazil only 15 per cent exhibit pulmonary involvement, whereas in Argentina up to 50 or 60 per cent are reported to show pulmonary involvement.

Most patients with the disease are agricultural workers or workers in the cotton industry.

A case is reported which occurred in a thirty-three year old mason. Three years previously the patient noted frequent upper respiratory infections, at times hemoptysis, followed by loss of weight. Extensive clinical examination was performed. Positive findings included increased erythrocyte sedimentation rate, fibrotic changes in the right lower lung field on the chest roentgenogram, and congested, infiltrated mucosa of the left lower and right middle lobar bronchi on bronchoscopy. Later, bilateral inguinal adenopathy and more pronounced bronchoscopic changes were observed. Biopsy of an inguinal lymph node resulted in a diagnosis of *Paracoccidioides brasiliensis* granuloma. Treatment included sulfa drugs, transfusion of blood and supportive therapy. Large mediastinal lymph nodes had compressed the trachea, necessitating tracheotomy and insertion of a cannula. The final outcome of the patient was quite favorable, the improvement being attributed largely to the administration of sulfadiazine.—*Charles Nice, M.D.*

KONAR, N. R., and SEN GUPTA, A. N. Splenic venography. *Brit. M. J.*, Oct. 10, 1953, *2*, 810–812.

Because of recent interest in the surgical treatment of cirrhosis of the liver, it has become increasingly important to determine patency of the portal and splenic veins preoperatively. Direct injection of these veins or tributaries requires laparotomy. However, in 1952, Dreyer and Budta-Olsen performed splenic venography in 11 cases without untoward incident and suggested that the method might be useful in finding the site of block in portal hypertension.

The authors have carried out splenic venography in 14 cases: 2 control cases, 2 with portal hypertension, 3 with cirrhosis of the liver, and 7 with splenomegaly of unknown etiology. Subsequent to these reported cases they have performed splenic venography on 9 other patients with no untoward incident.

The method used was as follows: The patients fasted overnight and were given 50 mg. pethidine hydrochloride half an hour before the procedure. With the patient supine on the roentgenographic table, the spleen was punctured through the left ninth intercostal space in the mid-axillary line under infiltration anesthesia with 2 per cent procaine. The ordinary lumbar puncture needle was used and 20 ml. of a solution of iodoxyl was injected into the splenic pulp in approximately five seconds. The patients were asked to hold their breath at the end of inspiration until the injection was completed. Most of them complained of pain over the spleen immediately after injection of the opaque medium, lasting five to ten minutes. There was some bleeding due to puncture of the spleen which usually stopped spontaneously, but the possibility of excessive bleeding and of rupture of the spleen exists and the procedure should be carried out only in a hospital where emergency splenectomy can be done.

The first exposure was made when 15 ml. of opaque medium had been injected and the next exposure five seconds later when the full amount had been injected. In a normal splenic venogram the splenic vein and the portal vein and its intrahepatic branches are visible. The contrast substance leaves the spleen very rapidly but a small residue may remain in the spleen even an hour after the injection.

In obstruction of the splenic vein the portion of the vein beyond the obstruction will not appear. In portal hypertension due to greatly increased pressure in the portal circulation, the blood flow may be reversed and the opaque medium may enter the inferior mesenteric vein, its tributaries, and the left gastric vein.

In cirrhosis of the liver the obstruction to the portal vein is inside the liver and the intrahepatic branches of the vein are either not made out or faintly seen, depending on the degree of obstruction. The extrahepatic portal vein and the splenic vein become markedly dilated and tortuous, but the inferior mesenteric and left gastric veins may not be demonstrated unless the portal hypertension is great. Hence, the degree of prominence and tortuosity of these veins in the splenic venogram will be a measure of the extent of portal hypertension.

In cases of splenomegaly of unknown etiology, the splenic vein carries a large amount of blood and becomes dilated and tortuous. The portal veins and intrahepatic branches also become dilated but due to dilution of the contrast substance the outlines are often faint. Inferior mesenteric and gastric veins are not seen, as there is no associated portal hypertension.—*A. B. Smith, M.D.*

MOESCHLIN, S., MARTI, H. R., and GERMANN, W. Tödliche Panmyelopathie durch Thorotrast (Thoriumdioxyd). (Fatal panmyelopathy due to thorotrast [thorium dioxide].) *Schweiz. med. Wchnschr.*, Oct. 31, 1953, *83*, 1061–1064.

This case report deals with a fatal aplastic anemia occurring seven years after intra-arterial injection of 30 cc. of thorotrast.

At autopsy the liver and spleen proved to be radioactive although the bone marrow was not. A long latent period of six to twelve years is characteristic of the damage which this contrast medium causes.

The authors conclude that thorotrast should not be used as an opaque substance for the demonstration of the liver and spleen or for arteriography.—*Albert Oppenheimer, M.D.*